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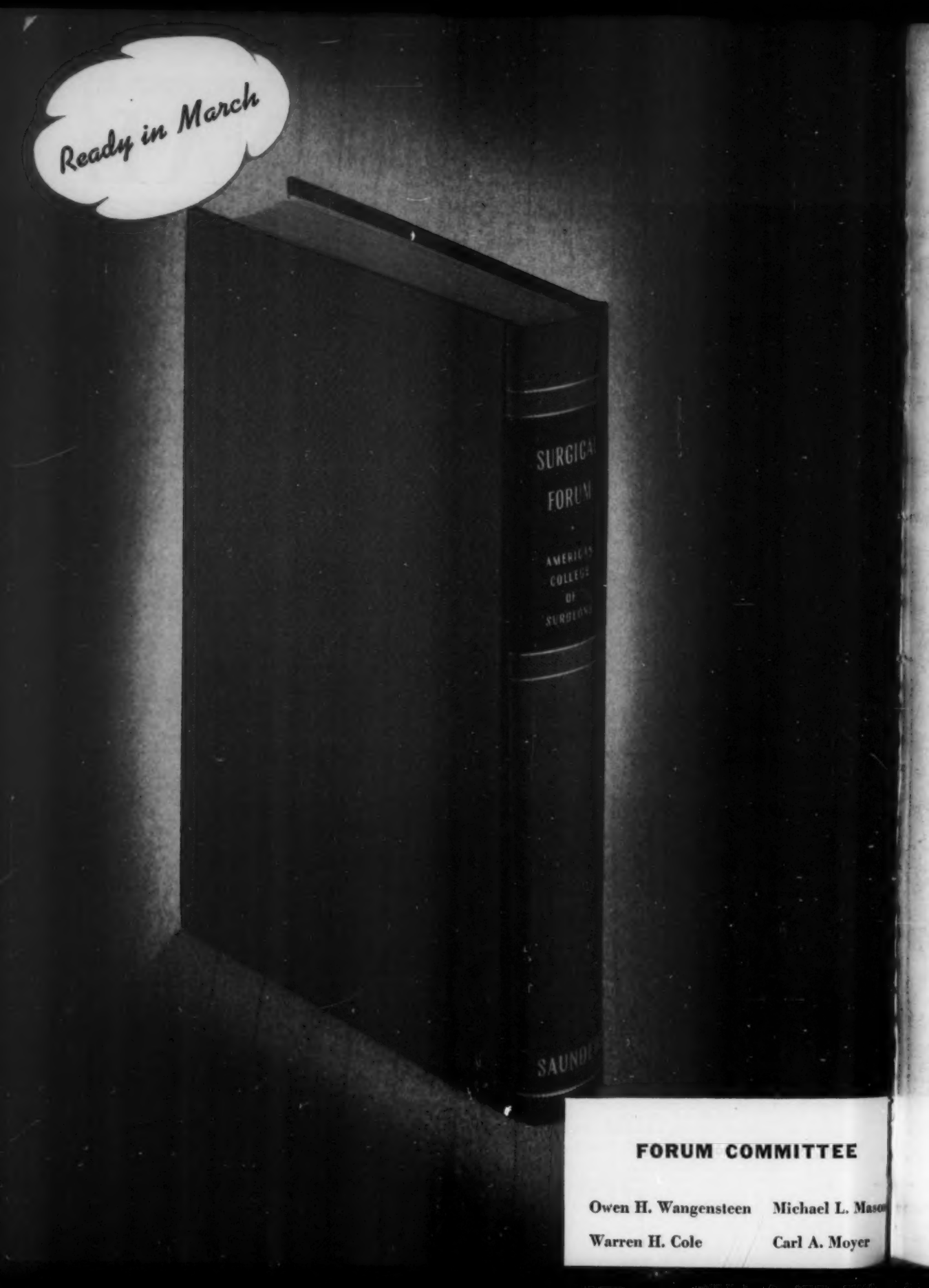

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ATOMIC ENERGY IN WAR AND PEACE

MEDICAL ASPECTS

Shields Warren, M.D., Boston

In this half-century year atomic energy has been available less than 10 years, but during that period it has grown to be a major force in research, in military strategy and in world politics. Hundreds of thousands of persons are concerned with one or another aspect of it directly, and hundreds of millions of persons are concerned with it indirectly.

It is well worth while for the medical profession to take account of the situation today and, in reviewing some of the lessons that have been learned, to try to foresee some of the problems of the future.

The development of the Atomic Energy Project, first in the Manhattan Engineering District and later in the Atomic Energy Commission, has given outstanding evidence that earnest and cooperative effort applied even to a virtually unknown problem of preventive medicine can result in the safe development of an enormous enterprise. By 1940 standards this enterprise would have been extremely hazardous, but it has a health record comparable with and even better than that of industries regarded as safe by ordinary industrial standards. This development has proved that with determined effort, energetic research, attention to detail and cooperation of employees an enviable record of safety can be maintained in a potentially dangerous industry. There still are to be solved some problems in permanent radioactive waste disposal, but these are relatively minor compared with the problems already overcome.

Some days ago I was reading a 30 year old report of the Huntington Memorial Hospital, in which one of the pioneers in biophysics, Dr. Duane, stated that a new era of progress was ahead in his field of work and that it might someday be feasible to irradiate tumors effectively with more intense and more deeply penetrating roentgen rays. He was thinking in terms of roentgen rays generated at a level of a few hundred thousand volts.

What would he think of the nuclear energies that can be provided today, when betatrons operating at energy levels of 20 mev and synchrotrons at 70 mev are available commercially?

Great progress has been made in the past years in radiation therapy, but not the spectacular and revolutionary advance of which some dreamed. Rather, there has been a slow accretion of knowledge, a gradual pushing back of the frontiers of ignorance.

Technical improvements in therapy with radioactive isotopes are steadily occurring. The principle of selective concentration of certain radioactive isotopes or compounds containing them by tumor tissue is important. However, any discovery of revolutionary importance in therapy is relatively unlikely.

For example, let us consider briefly the relative advantages and disadvantages of radium and its isotopic substitute, radiocobalt. In the 50 years since the discovery of radium, that element has attained a role of major importance in cancer therapy, as well as being useful in the treatment of a number of dermatological conditions of minor importance. By virtue of the emission by radium of the poorly penetrating but heavily ionizing alpha particles, of the more penetrating but significantly destructive beta particles and of the deeply penetrating gamma rays, the element can be used unfiltered for extremely superficial treatment and filtered for more penetrating or for interstitial radiation, subject of course, to the limitations of the inverse square law. Its gaseous disintegration product, radon, provides extraordinary flexibility for therapy, because the compressibility of radon, existing as it does in a gaseous state, permits the preparation of sources with varying activity as related to size. Moreover, the short half-life of radon, 3.9 days, enables it to be utilized interstitially with assurance that the desired dose can be given in not too prolonged a period. Appropriately screened radon is a virtually pure gamma ray source. As a result of these and other virtues, radium became a part of the standard armamentarium of those interested in cancer therapy and related fields.

Radiocobalt emits no alpha particles, gives off a weak beta radiation which may be easily screened out and gives a gamma radiation similar to that of radium, with an average of 1.2 mev, as compared with that of radium, with an average of 0.6 mev. If irradiated a sufficiently long time in the atomic pile, radiocobalt

Director, Division of Biology and Medicine, United States Atomic Energy Commission.
Read in the General Scientific Meetings in the Atomic Energy Commission Symposium at the Ninety-Ninth Annual Session of the American Medical Association, San Francisco, June 26, 1950.

can be made not only as radioactive as radium but even more so, milligram for milligram. While the half-life of radiocobalt of 5.3 years means that its useful life is far less than that of radium with a half-life of 1,590 years, nonetheless this is not a great handicap, since radiocobalt can be produced in the chain-reacting pile much more cheaply than radium can be separated from the ore in which it occurs.

From the standpoint of medical research, atomic energy and its products offer a program of such intense promise that it cannot help having an impact on each university and each hospital in the country. Those engaged in and profiting by the results of medical research in their practice are now within the threshold of an era that promises to outstrip the great surges of advance already recorded in medical history. The use of radioactive tracers available in a multiplicity of forms has virtually revolutionized many technics and has brought some problems that seemed difficult or impossible to solve by other technics within the possibility of solution.

There is hardly a research journal in the fields of medicine or biology that one can pick up today without finding in it articles presenting the advances made by the use of the tracer technics. Whether one is interested in the localization of brain tumors, circulation time or synthesis of proteins, he finds in the radioactive isotopes tools ready for his hand.

How different the rest of this paper would be if the United Nations had achieved the objectives hoped for by its founders. Since it has failed to produce the hoped for utopia and since the cold war is a harsh reality, one must think of the potential wartime uses of atomic energy and the problems that they create.

Atomic defense cannot be considered apart from civil defense problems in general. The governmental agency concerned with civil defense planning is the National Security Resources Board.[1] The Atomic Energy Commission together with other agencies provides the board with such information as may be pertinent to it in its planning capacity. Doubtless some wonder impatiently why plans in this phase of the problem appear so slow in culmination. Perhaps the greatest detriment to planning lies in the fact that serious decisions regarding conduct in time of war are extremely delicate and difficult to make in time of peace.

You may remember the boy who was given a job in a market at man's pay. All he had to do was to sort potatoes into two piles, the large here and the small there. Although he started his first day enthusiastically, before noon he came into the office and resigned. His astonished employer, asking the reason, was enlightened by the boy as follows: "I like you all right, Mr. Jones. This is a nice store and the pay is very good, but these decisions, they're killing me!"

Translate this boy's predicament into terms of the unprecedented degree of importance of each phase of complex peacetime planning for war, and one can readily appreciate the delicacy with which each step to be taken in civil defense planning now must be made.

1. The Civil Defense Administration was established Dec. 1, 1950.

Fortunately, the American Medical Association has not been lagging, and the Council on National Emergency Medical Service of the American Medical Association has planned a program of action that should be of material aid in the solution of the complexities ahead. This program of the Council deserves reiteration:

1. Emergency medical service committees would be established in each state medical society.

2. Each state would urge its governor to appoint a state director of civil defense, with the necessary responsibilities and authority to act.

3. Each state would appoint a civil defense advisory committee to advise its governor and the civil defense director. Representatives of state medical societies should with advantage serve on this advisory committee.

Appraisal of the existing facts is helpful. At present there are 160,000 physicians and some 6,000 approved hospitals scattered among potential target areas. Too many of the hospitals are closely localized in prime target areas.

The will to do what is necessary is strong among our people. It is heartening to know that in the recent South Amboy disaster many of the former members of the wartime civil defense automatically went to their former posts to carry out the duties that might be assigned to them.

A defeatist attitude on civil defense will get us nowhere. The problem is not hopeless. The initial steps in the provision of knowledge concerning medical aspects of atomic warfare and the means of monitoring a radioactive disaster have already been taken.

The need for further accomplishment is clearly before us, but let us remember that atomic energy has its values as well as its handicaps, its aid to healing as well as its power to kill.

Endocrine Therapy of Cancer of Breast.—Endocrine therapy is a new agent in the treatment of breast cancer, and occasionally it can confer great benefits. At the present time, however, there is no place for the endocrine treatment of any patient with malignant disease of the breast if she is treatable either by surgery or by radiotherapy. This statement is based on the evidence that no patient has been "cured" by estrogens or androgens, even in the limited sense that five years after treatment, disease cannot be detected. A few patients may survive in good general health for this period or longer, disease always being present, and in view of the varying natural history of mammary cancer it is impossible to tell how long they would have lived without any treatment. It is true that all the experience has been gained on patients whose disease is advanced when first seen, or in whom recurrence has occurred after treatment by surgery or radiotherapy. Nevertheless, I feel that it is unjustifiable to treat an early case of breast cancer with estrogens or androgens.

The situation is different when the treatment of advanced cancer is concerned. In cases which are beyond surgical treatment or radiotherapy even in a palliative sense, the sex hormones play a role as palliative agents in about 25 per cent, of late cases, and are also of considerable theoretical interest in the study of malignant disease of the breast.—Edith Paterson, M.B., *The Practitioner*, November 1950.

ACUTE RADIATION SYNDROME

A PROBLEM FOR PRACTITIONERS

John Z. Bowers, M.D., Salt Lake City

The terms atomic energy, radiation and radioactivity all refer to the particles and electromagnetic radiations which are liberated from the nucleus of the atom as a natural phenomenon or by artificial processes. In the explosion of an atomic bomb, vast numbers of such particles and rays are released from the atoms of plutonium or uranium. Several of these penetrate the body with ease and cause injury to the cells that lie in or near their path. The purpose of this report is to restate the changes that are known to occur in the body as the result of exposure to large amounts of such penetrating atomic energy and to emphasize the fact that the resultant signs and symptoms are sufficiently unique and recognizable to warrant the inclusion in the nosology of every physician of a specific disease entity, the acute radiation syndrome. A knowledge of the new nuclear physics is not necessary for an understanding of the clinical problems encountered.

DEFINITION

The acute radiation syndrome is caused by the exposure of the whole body to damaging amounts of penetrating radiation, resulting in acute degenerative changes in the blood and the blood-forming organs, the blood vessels and the bowel and characterized clinically by prostration, a hemorrhagic diathesis, nausea, vomiting, diarrhea and epilation. The treatment is at this date supportive, and the outcome without treatment is often fatal.

As is well known, there have been two explosive outbreaks of the disease, one occurring in Hiroshima, Japan, on Aug. 6, 1945, and the other in Nagasaki, Japan, on Aug. 9, 1945. The exact incidence of the disease among the people injured in these blasts is not well known; there were many persons who died from trauma or burns before the signs, symptoms and pathological changes characteristic of the disease had developed. Generally accepted estimates are that of the 100,000 fatalities, about 15,000 actually died of the acute radiation syndrome.

ETIOLOGY

It is important to realize that all forms of atomic energy generally affect tissues and cells in the same way. The difference is one of quantity rather than quality, according to the specific damaging ability and the degree of penetration of the particular particle. In the explosion of an atomic bomb at the height of several thousand feet, gamma rays and neutrons are the liberated energies of concern. Gamma rays are similar to roentgen rays—that is, they are highly penetrating and moderately damaging. Neutrons are both highly damaging and highly penetrating. At Hiroshima and Nagasaki, there was no evidence of residual contamination that would be a health problem; the damaging radiation was liberated in a very transient wave or burst.

The rapidity with which typical clinical manifestations develop is, in general, proportional to the severity of the exposure.

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Read in the General Scientific Meetings in the Atomic Energy Commission Symposium at the Ninety-Ninth Annual Session of the American Medical Association, San Francisco, June 26, 1950.

PATHOGENESIS

The particles and rays liberated in the explosion of an atomic bomb in the air carry a considerable store of energy and, with the secondary particles and rays which they incite, release this energy into the cells in their path as they pass through the body. As a result, the chemical compounds of which the cells are composed undergo profound changes and the cells are often unable to survive. One particle or ray is capable of injuring a number of cells irreparably. However, even in death there remains the basic substance from which future cells may spring, and thus in time the cells which have been damaged will be replaced. Present therapeutic programs are based on this inherent ability of the damaged tissue to replace itself.

When the cells of the body grouped into functional tissues are considered, it is found that there is considerable variation in the sensitivity of specific tissues to radiation injury. The basic premise on which a clinical approach to this problem should be based is that the blood, the blood-forming organs, the blood vessel endothelium and the bowel are the tissues which are the most severely damaged. The germinal epithelium and the lymphatic tissues also show pronounced changes but probably do not contribute so significantly to the clinical picture. Other tissues such as muscle, brain and nerve are relatively resistant to radiation injury; indeed, in a patient who has died from acute radiation injury, there may be no evidence of pathological alteration in these organs. Lung, liver and kidney occupy an intermediate position. Again, one must remember that the blood and the blood-forming organs, the blood vessel endothelium and the bowel are the injured tissues that serve as a basis for the signs, the symptoms, the treatment and probably the complications of this important disease.

When the tissues of the body grouped to form an individual are regarded, again a factor of variation in sensitivity is found entering into the considerations of the problem. This is best evidenced by the fact that a radiation exposure fatal to one person may cause only a moderate reaction in another, particularly one who exhibits the hemorrhagic or pancytopenic form of the syndrome. Undoubtedly a person who is suffering from the fulminating form of the disease has received such massive exposures that a sensitivity factor does not apply.

PATHOLOGY

The primary effect of radiation on the cells of the body is a cessation of mitotic activity, as a result of which cells die and are not immediately replaced. The

time required for this destruction to become histologically, and therefore clinically, evident depends in part on the life span of the cell in question. Thus the cessation of mitotic activity by the leukopoietic tissues results in leukopenia within 24 hours, owing to the short life span of the leukocyte.

On the other hand, the erythrocyte has a life span of about 100 days, and anemia is the last of the hematological alterations to appear. In the usual case, at the height of the illness, the hematopoietic tissue has almost completely disappeared from the bone marrow. The reticulum cells, however, remain active,[1] and it is probable that from these progenitors replacement blood cells spring. Subsequently the marrow may assume a hyperplastic picture with obvious maturation arrest—obvious because, despite the overactivity in the marrow, there is a marked deficiency of peripheral blood cells. There is also a rapid disappearance of lymphoid cells.

Changes in the gastrointestinal tract, from focal ulceration to extensive sloughing, are restricted primarily to the mucosal surface and probably represent a combination of effects of radiation and the rapid invasion of micro-organisms. A similar basis is applicable to the extensive ulcerative lesions of the oral and pharyngeal membranes.

Although the gonadal tissues do not contribute to the clinical syndrome, mention should be made of the extensive destruction of the germinal epithelium in the male; changes in the female gonads are not so pronounced.

CLINICAL HISTORY

Three forms of the syndrome can be categorized.

1. The fulminating form is seen in persons who have received overwhelming injury and in whom a fatal outcome is assured, usually 7 to 10 days after exposure. The march of signs and symptoms is steadily progressive from onset until death. Vomiting appears within 12 hours of exposure, to be joined in 24 hours by prostration, fever and diarrhea. Petechiae and purpura are first manifest at about five days,[2] at which time there develops a rapid and steplike rise in temperature. The increasing weakness becomes extreme and is associated with tachycardia and hypotension. The profuse diarrhea, which often becomes bloody, contributes to the dehydration, which is increasingly evident. Examination of the blood reveals progressive leukopenia that may reach levels of 400 to 500 cells per cubic millimeter. The red blood cell levels usually remain normal, but thrombocyte (platelet) levels are depressed.

2. The hemorrhagic form of the disease is seen in patients who have received extensive but not necessarily fatal injury. Death, if it is to be the result, usually occurs in three to four weeks. Within 24 hours of exposure, nausea, vomiting and diarrhea with prostration usually appear and persist for 24 hours. The person is then generally well for 10 days to two weeks, at the end of which time epilation of the scalp occurs. Coincidentally there occur increasing weakness and malaise and the appearance of extensive petechiae and purpura patches, which may be associated with gross bleeding from body orifices or from the ulcerative These bear a striking resemblance to the lesions which lesions which rapidly appear in the mouth and pharynx. characterize agranulocytic angina. Gastrointestinal disturbances, of which diarrhea is the most pronounced, reappear and are joined by fever. A majority of the patients in this group die in three to six weeks after the initial exposure unless treatment is energetically pursued. Others enter a more chronic course with continuing ulcerative lesions and anemia, while recovery slowly occurs in a third group.

3. The pancytopenic form of the disease occurs in persons who have been less severely exposed. Some show initial nausea, vomiting and mild prostration, with or without a transient diarrhea. The entire initial reaction is relatively brief (about 12 to 24 hours) and mild; it does not occur in a considerable number of the patients in this group. Three to five weeks after this initial exposure, epilation occurs, to be followed by mild inflammation of the oral and pharyngeal membranes and weakness with malaise. Nonsanguineous diarrhea frequently develops. The hematological changes in these patients are often those of severe and increasing anemia. The vast majority of the fatalities are due to aplastic anemia, with death occurring two to four months after the initial exposure. In contrast to the hemorrhagic variety of the disease, petechiae, purpura and the like do not form so significant a part of this picture. A large number of patients in this group recover.

SIGNS AND SYMPTOMS

With these varying clinical courses in mind, attention may now be directed more specifically to the signs and symptoms of the syndrome. There are three manifestations of acute radiation injury which are sufficiently unique to warrant repeated emphasis as a clinical triad representing the disorder—namely, hemorrhagic diathesis, epilation and gastrointestinal disorders (nausea, vomiting and diarrhea), developing from damage to the blood and the blood-forming organs, the blood vessels and the bowel.

The hemorrhagic diathesis is the summation of three pathological effects of radiation: thrombocytopenia, increased porosity of the smaller blood vessels and appearance in the peripheral blood of a circulating anticoagulant resembling heparin. It includes petechiae, purpura, melena, epistaxis, metrorrhagia and, at times, gross bleeding from other mucosal or débrided surfaces. The earliest appearance has been reported at four days after exposure, while in milder cases it may be delayed until the fourth week of the illness. In appearance the petechiae and purpuric lesions resemble closely the lesions encountered in rickettsial disease or in meningococcemia.

1. Liebow, A. A.; Warren, S., and De Coursey, E.: Pathology of Atomic Bomb Casualties, Am. J. Path. 25: 853-1027, 1949.

2. Leroy, G. V.: Medical Sequelae of the Atomic Bomb Explosion, J. A. M. A. 134: 1143-1148 (Aug. 2) 1947.

Epilation may occur in the second to the fifth week following exposure, ordinarily in 14 to 20 days. In the fulminating form of the disease, death usually ensues before sufficient time has elapsed for the extrusion, with failure of replacement, of the hair. The loss is usually restricted to the scalp, begins on the crown and produces a distinctive appearance that Leroy has compared to a monk's tonsure. Regrowth of hair usually begins in seven weeks to three months, and the replacement is ultimately complete. Shields Warren has pointed out that in the pancytopenic form of the disease the duration of the epilation may be a helpful prognostic sign, in that those patients who continued bald died while those who recovered showed a rapid regrowth of hair. The appearance of epilation in a suspected person is presumptive evidence of radiation injury and usually ushers in the hemorrhagic form of the disease.

Nausea, vomiting and diarrhea represent presumptive evidence of radiation injury, especially diarrhea. The temporal relationship of the latter varies considerably, for in the fulminating form of the disease, diarrhea occurs within 24 hours of exposure and continues throughout the rapidly progressive downhill course. In the hemorrhagic form of the disease, diarrhea accompanies the initial reaction, but gastrointestinal functions then become clinically normal until the onset of the full-blown clinical picture of hemorrhagic diathesis and epilation. The stools are watery, contain large amounts of mucus and may be bloody. The severe dehydration which occurs in the disease is undoubtedly related to the heavy loss of salt and water that occurs through the gastrointestinal tract.

Infection in a variety of forms plays an important role in the hemorrhagic variety of the disease; indeed, the situation is unusually favorable for its occurrence. The denuded gastrointestinal surfaces afford easy access for the organisms ordinarily harbored in that tract. The agranulocytic ulcerations in the mouth and neighboring structures afford a second potential portal of entry. The defenses of the body are lowered by the agranulocytosis, which is very pronounced. The importance of infection has been verified by Howland [3] in dogs and by Miller [4] in mice, in which the administration of antibiotics favorably affects the course of the disease.

Hematological manifestations of acute radiation injury are better understood than other effects. In animals and patients an initial transient leukocytosis often occurs within a few hours after total body irradiation. The subsequent pronounced fall in the white blood cells may occur as early as the second day and is evident in all forms of the disease. The lymphocyte is the most sensitive cell in the body and is depressed quite early. The thrombocytes (blood platelets) fall within the first week in the fulminating form and in the second to third week in the hemorrhagic form. Anemia does not appear before the seventh day, is constantly the last of the hematological manifestations to become evident and is likewise the last to return to normal. Peripheral manifestations of recovery of leukopoietic functions may become evident at the sixth week, while in the marrow evidences of recovery appear as early as the seventh day in the most severely injured patients.

SEQUELAE

Experience accumulated from studies in animals suggests that genetic aberrations, blood dyscrasias, neoplasia and cataract formation are the sequelae that may possibly develop. Studies on the Japanese survivors are being carried out by the Division of Medical Sciences of the National Research Council, under the sponsorship of the United States Atomic Energy Commission, for the purpose of gathering all possible information relevant to these problems. Thus far there has been no evidence of an increased incidence of genetic mutation, blood dyscrasia or neoplasia. Cogan, Martin and Kimura [5] report that 10 instances of radiation cataract have appeared in the Japanese survivors; all these survivors were within 1,000 meters of the hypocenter. One thousand persons who were within 2,000 meters of the hypocenter have been examined and show no evidence of lenticular opacity. Instances of cataract appearing in scientists who had worked with cyclotrons have also been reported and bear on the general problem.[6]

COMMENT

This report has not attempted a comprehensive coverage of the literature on the acute radiation syndrome; rather, it has attempted to extract and emphasize those points which seem most pertinent to an understanding of the disease by the physician who with the pressures and problems of practice is concerned with that knowledge which will implement his ability to handle such cases.

SUMMARY

The pertinent information that has been presented may be summarized as follows: The acute radiation syndrome is caused by sudden exposure to the penetrating radiations liberated by the atomic bomb. The resulting changes depend primarily on the inherent sensitivity of the exposed tissues and the type of radiation and are attributable to damage to the blood and the blood-forming organs, the blood vessel endothelium and the bowel. These particular tissues all show a tendency toward ultimate regeneration, and it is on this fact that present therapeutic programs are based. The primary manifestations are hemorrhagic diathesis, nausea, vomiting and diarrhea and depression of the formed elements of the body. Treatment is at this date supportive in nature.

3. Howland, J., and others: Studies on Factors Effecting the Radiation Syndrome: I. The Effect of Aureomycin and Antibiotics on Whole Body Radiation, UR 94, United States Atomic Energy Commission, Oak Ridge, Tenn., Nov. 2, 1949.

4. Miller, C. P.; Hammond, C. W., and Tompkins, M.: Reduction of Mortality from X-Radiation by Treatment with Antibiotics, Science **111**: 719, 1950.

5. Cogan, D. G.; Martin, S. F., and Kimura, S. J.: Atom Bomb Cataracts, Science **110**: 654, 1949.

6. Abelson, A. H., and Kruger, P. G.: Cyclotron-Induced Radiation Cataracts, Science **110**: 655, 1949.

RECENT ADVANCES IN DIAGNOSIS AND TREATMENT OF DEFICIENCY DISEASES

Tom D. Spies, M.D., Chicago

For the past twenty years I have been interested in the relationship of diet to disease. Great advances have been made in the recognition of dietary deficiences, and dramatic results have been observed following the persistent application of adequate amounts of specific therapeutic agents. The number of cases of pellagra, beriberi, scurvy and rickets has been decreased dramatically; in fact, these diseases have been almost eradicated from the United States.

My experience in the diagnosis of nicotinic acid (niacin) deficiency, ascorbic acid deficiency, thiamine deficiency and riboflavin deficiency recently has been discussed at considerable length.[1] I realize that the methods of diagnosis and treatment described are still not perfect, but they are the best available and I can recommend no better means of relieving persons with deficiency disease. It is obvious that an accurate diagnosis is essential for proper treatment. Yet, after twenty years of concentrated study in this field of medicine, I still find it more difficult to diagnose atypical manifestations of these diseases than I do to diagnose the usual case of tuberculosis, heart failure, leukemia or other general medical diseases. Among the many thousands of patients whom I have examined I have not seen two patients with identical signs and symptoms of nutritional deficiency disease, which shows the great variation in the manifestations of these disease complexes. From the standpoint of practical therapeutics the practicing physician, from time to time, comes face to face with the difficult task of proper diagnosis and treatment of men, women and children whose tissues are injured by undernutrition or malnutrition. It is important for him to have in mind that nutritive failure is characterized by a mixture of deficiency diseases operating simultaneously and that it is necessary to make a precise diagnosis or precise diagnoses and then apply complete therapy which will insure full rehabilitation of the patient.

CLINICAL OBSERVATIONS

The patient whose picture is reproduced in figure 1 obviously has nutritive failure. He has eaten a diet deficient in many precious nutrients. One of my patients, M. D., a little girl with bilateral cheilosis, had nutritive failure, as did the other members of her family. (The dogs that ate scraps from the table also had dietary deficiency diseases, which gives an idea of the general nutritional situation in the family.) Under the supervision of Miss Jean Grant, head dietitian of the Nutrition Clinic, Hillman Hospital, the nutrient value of the food which was being eaten by this family was determined experimentally.

Sixty 30 day old male albino rats of the Sprague-Dawley strain were selected and divided into three groups of 20 each. The basal diet allowed the three groups of rats for a period of eighty days was identical in composition to that eaten by the family (see fig. 2). It contained approximately 35 per cent cornmeal, 28 per cent white flour, 19 per cent sugar and 18 per cent refined fats. These foods were mixed with enough water to form a thick paste, which was then oven dried and ground to a coarse powder. The food was given to each rat mixed with enough water to form a batter-like mass. The condition of the rats in group 1, which received the basal diet only, showed that the diet consumed by this family was inadequate to support the growth and health of normal young rats. The rats in group 2 were fed the identical diet but, in addition, received each day a supplement of vitamin-free casein and a salt mixture. The salt mixture contained calcium carbonate, dibasic potassium phosphate, dibasic calcium phosphate, magnesium sulfate, sodium chloride, ferric citrate, potassium iodide, manganese sulfate, zinc chloride and copper sulfate. The rats receiving the basal diet plus casein and minerals were healthier and much more vigorous than those of group 1 but still did not grow as well or look as well as those in group 3, which received synthetic vitamins in addition to casein and minerals. Certainly these studies indicate that the family's diet lacked proteins, minerals and vitamins essential for the proper growth of healthy young rats.

After studying the foods composing the diet of this family and after administering them to animals in the laboratory, we decided to study the effect of a supplement in 1 quart (1,000 cc.) of milk on the growth of one of the six children in the family, the child with bilateral cheilosis. Her case history follows:

M. D., the sixth child in the family, was born in September 1935. Although the mother felt well while carrying M. D., the child was small and weak at birth. She was breast fed until she was 2 years of age, when her mother became pregnant again. According to her mother, the girl at the age of 2 years was "pale, had no blood and didn't feel good enough to be fussy." A physician prescribed "blood medicine and orange juice" for her at this time. As the child grew older she became highly nervous and sensitive.

At the time I first saw the family in 1940, when the girl was 5 years of age, she appeared to be "nervous to the point of hysteria." For the first nine months of my frequent visits to her home she hid under the bed or went into the woods at my approach. She had nightmares, "cried all the time" and her appetite was poor. Figure 2 indicates how inadequate her diet was at this time in the essential nutrients. She complained of her eyes burning, her legs aching and frequent headaches and backache. She was underweight and pale. Cheilosis was present at both angles of the mouth. There were small discrete areas of erythema over the sides and tip of the tongue. These areas were typical of pellagrous glossitis, and they disappeared in 12 hours after the administration of 200 mg. of nicotinamide (niacinamide) administered orally in divided doses.

In the spring of 1941 she was given small amounts of dried (brewer's) yeast and yeasted peanut butter, and she showed great improvement. She was no longer apprehensive. Instead of crying or hiding at my approach she smiled and gradually became friendly. Her mother said that the child rested more, had a better appetite and had gained a little weight. The cheilosis decreased but did not disappear.

Head of the Department of Nutrition and Metabolism, Northwestern University Medical School.

Read before the Joint Meeting of the Section on Gastro-Enterology and Proctology and the Section on Pathology and Physiology at the Ninety-Ninth Annual Session of the American Medical Association, San Francisco, June 30, 1950.

The material is from the Department of Nutrition and Metabolism, Northwestern University Medical School, Chicago, and studies in nutrition at the Nutrition Clinic, Hillman Hospital, Birmingham, Ala., and at the General Calixto García Hospital, Havana, Cuba.

The anemia studies were made possible by a grant from Lederle Laboratories; the rehabilitation studies done in Birmingham, Ala., were aided by a grant from the Birmingham Citizens Committee; the tropical malnutrition studies were supported by a grant from Fundación de Investigaciónes Médicas, and the studies in Birmingham on the growth and development of children were aided by a grant from the American Dry Milk Institute, Inc.

1. Spies, T. D.: Rehabilitation Through Better Nutrition, University of Cincinnati Studies in Nutrition at the Hillman Hospital, Birmingham, Ala., Philadelphia, W. B. Saunders Company, 1947.

In June 1941 a roentgenogram of this child's wrist indicated that she was a year behind schedule in bone development. She was a short, somewhat slender child who was maturing at an exceedingly slow rate.

In July 1941 she was given synthetic riboflavin, 5 mg. orally three times a day for 30 days, and she improved. Her eyesight became better, and the cheilosis disappeared. Her general condition remained somewhat the same until 1945, when it became possible to give her a milk supplement.

From April 1945 until December 1946 she received the equivalent of 1 quart of nonfat milk daily, six days a week, an amount which supplied: total calories 305.6; protein 31.4 Gm.; calcium 1.1 Gm.; phosphorus 0.64 Gm.; thiamine 0.3 mg.; riboflavin 1.73 mg., and niacin 0.79 mg. During this period of time there were only seven days on which she was scheduled to get the milk supplement that she did not drink it. Physical examination at the beginning of this period showed that she was poorly developed, poorly nourished and appeared chronically ill. Her expression was anxious and her

Fig. 1.—J. McC., a white man with nutritive failure.

complexion sallow. There was slight injection of the conjunctivas. While she was receiving the milk supplement she contracted erysipelas and colds but none of the diseases of childhood. Her appetite was fairly good and frequently she even complained of being hungry.

When the milk supplementation was begun, the physical status of the child was fair but her rate of progress was slow. When we decided to give the milk supplement we knew it was not possible to correct the whole caloric deficit with a single quart of nonfat milk daily, but we wished to see whether it would benefit the child (see fig. 3). After she completed the period of milk supplementation, some of those who knew her well made the following comments about her: Her mother said, "After drinking the milk my daughter felt better, slept better, did not have so many 'nightmares,' helped around the house, was less nervous, did not cry so much and was a happier child." Her teacher said, "She was less tired, had more energy and was less nervous after drinking the milk. She made excellent grades. Her conduct and attitudes were extremely good."

The social worker observed, "Except for erysipelas and slight colds at the beginning of the milk period, the child's only troubles were two minor stomach upsets. Her colds became less severe and were of shorter duration after she had been receiving the milk for three months. Within a few weeks after the milk supplement was discontinued, she became apprehensive, nervous and as easily disturbed as she had been before receiving the milk supplementation."

Roentgenograms during this period indicate that the significant change in her bone growth was the narrowing of her zone of asymmetry in joint surface production.

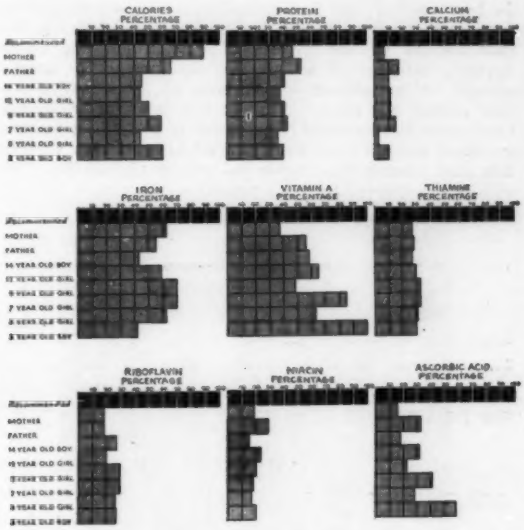

Fig. 2.—Nutrients supplied by dietary of the D. family contrasted to allowances of nutrients recommended by the Committee on Foods and Nutrition, National Research Council.

The child had a nicotinamide deficiency which was relieved by the administration of nicotinamide and a deficiency of riboflavin which disappeared after riboflavin therapy. She also had general nutritive failure which we combated at one time by dried brewers' yeast powder, at another by yeasted peanut butter and at still another time by nonfat milk solids. It is probable that

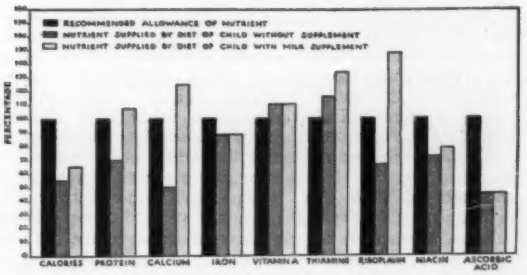

Fig. 3.—Nutrients supplied by diet of child M. D. (based on daily food intake for one week during spring, summer, autumn and winter) without and with supplement of dry nonfat milk contrasted to recommended allowances of nutrients.

the retardation of growth in the child was similar to that in the rats when they were fed a diet similar to that on which the child subsisted. For full growth and development she would require payment of the caloric deficit and a balanced diet for a long period of time.

J. McC., the man with undernutrition shown in figure 1, on physical examination was a pale, emaciated, weak person who appeared extremely apprehensive and who had pitting edema of the ankles (fig. 4). It was obvious from examination of the skin, mucous membranes, conjunctivas and nail beds that he had anemia. Anemia to me is always secondary. This man's anemia was really a symptom and not a disease in itself: the smooth, atrophic, pale tongue was a symptom and nothing more. In figure 5 it can be seen that the red blood cell count was close to 2,000,000, that he had a high color index and few reticulocytes. He had megaloblastic arrest of the bone marrow, and free hydrochloric acid, pepsinogen and rennin were present in the fasting specimen of the gastric juice. From all the stigmas of malnutrition—the severe diarrhea, the type of anemia and the presence of normal enzymes in the stomach—a diagnosis of nutritional macrocytic anemia was made. Since he had this type of anemia, I now knew that he would respond well to potent liver extracts, powdered stomach (ventriculin®), dried brewers' yeast powder, folic acid, vitamin B_{12}, vitamin B_{12a} and/or vitamin B_{12b}. We

Fig. 4.—Edema of legs, feet and ankles of J. McC.; note pitting.

decided to give him synthetic folic acid (Lederle). This substance is sometimes called by the biologist liver Lactobacillus casei factor and by the chemist pteroylglutamic acid. In nature it is found chiefly in conjugated form. Much of it occurs conjugated with seven molecules of glutamic acid (the B_c conjugate, a pteroylhexaglutamylglutamic acid). The administration of the conjugated forms is followed by a hematological and clinical response similar to that which occurs when free folic acid is given. The B_c conjugate is present in yeast, liver and other foodstuffs. The hemopoietic response that occurred in this patient following the administration of 5 mg. of folic acid by mouth daily for eight days is shown at the left side of figure 5 and is characteristic. There is an increase of reticulocytes in the peripheral blood and a subsequent increase in red blood cells, hemoglobin and platelets. There is a terrific outpouring of cells and materials from the relatively few megaloblasts in the bone marrow. It is one of the most impressive biological facts known to physicians. If this perfectly normal and necessary process could be understood, much about cellular growth in general would become clear.

2. Tomac® is manufactured by the Vital Foods Corporation and was supplied by Foster G. McGaw, American Hospital Supply Corporation, Evanston, Ill.

The first evidence of clinical response, which occurs when the reticulocytes in the peripheral blood begin to increase, is the occurrence of a sudden and striking increase in appetite which results in the patient eating large amounts of food he previously had refused (see fig. 6). This is accompanied with a great increase in strength and vigor; patients who have been extremely weak suddenly begin walking around the ward and helping in the care of other patients. At about the time the blood begins to show improvement the alimentary tract

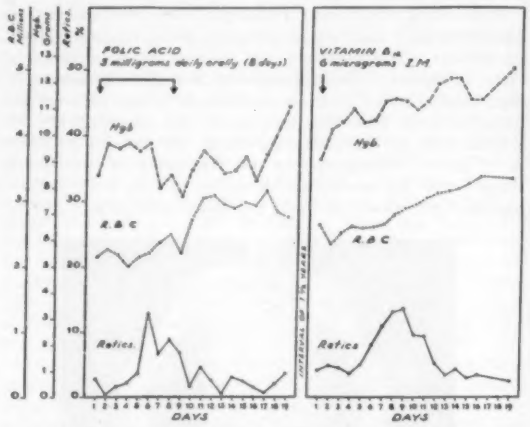

Fig. 5.—Comparative hemopoietic response of man with nutritional macrocytic anemia (J. McC.) to folic acid and vitamin B_{12}.

begins to return to normal. The glossitis begins to fade, and the stools tend to become more nearly normal. The patient's stool was liquid before therapy. One week after treatment with folic acid was initiated, the difference in the amount of material and in the consistency was remarkable. He gained strength rapidly, and the edema decreased. Eleven days after folic acid therapy was discontinued the blood values were: red blood cells 2,700,000; hemoglobin 11.1 Gm. (72 per cent), and reticulocytes 3.1 per cent. Although the blood levels were still below normal range and the edema had not subsided entirely, he wished to go home because of the illness of one of his children. Therefore he was given instruction in regard to the foods he should eat and was discharged from the hospital.

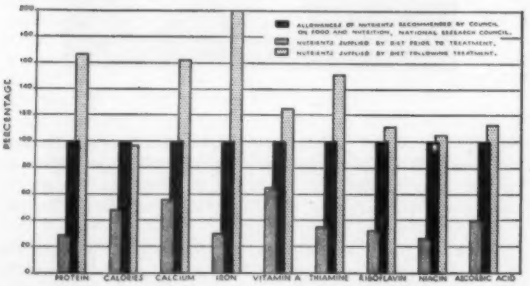

Fig. 6.—Nutrients supplied by diet of a patient (J. McC.) with nutritional macrocytic anemia before and after folic acid therapy contrasted with the recommended allowances of nutrients.

He returned to the Clinic the following week; the blood values had increased, but slight edema of his feet and ankles persisted. An evaluation of his diet showed that it still was inadequate, especially in protein content. Accordingly, he was given approximately 2 ounces (56 Gm.) of Tomac,® an oral protein supplement,[2] mixed with the equivalent of 1 pint (500 cc.) of nonfat milk daily. This was given at his home under supervision. The effect of this mixture on his daily intake of nutrients is shown in figure 7. Within a week the

edema had disappeared and he had gained 3 pounds (1.3 Kg.) in body weight. The protein supplement and milk mixture was given to him for a month. By the end of this time he had no evidence of edema and had gained 9 pounds (4.1 Kg.). He returned to his work as a farmer, ate a liberal, well-balanced diet and worked regularly for 10 months. Then he became careless about his diet and again began subsisting chiefly on food high in carbohydrate and fat. Within six months he became too weak to continue working; a month later, when severe diarrhea developed, he came to the Clinic seeking treatment. This time he did not have pitting edema. His blood values at this time can be seen at the right side of figure 5. It was decided to give him a single injection of 6 micrograms of vitamin B_{12}. His hemopoietic response to this therapy also is shown in figure 5, and it is similar to that which followed folic acid therapy. His clinical response likewise was similar.

FOLIC ACID AND VITAMIN E_{12}

The fact that the same patient responds to either folic acid or vitamin B_{12} requires a discussion of both these materials. The story of folic acid and the vitamin B_{12} family of vitamins is not complete. Nevertheless, the chemical, physiological and therapeutic developments already are so extensive that a book could be written about each.

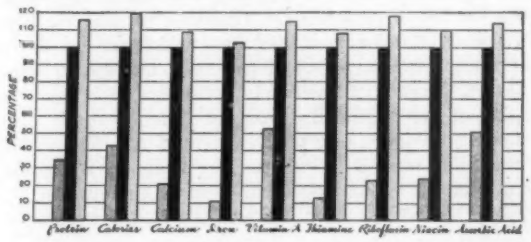

Fig. 7.—Nutrients supplied by diet of a patient (J., McC.) with nutritional macrocytic anemia before (shaded columns) and after (dotted columns) the addition of a protein supplement. Before the addition of the protein supplement all the protein in the diet was from vegetable sources. With the addition of the protein supplement 15 per cent of the protein in the diet was from vegetable sources and 85 per cent was from animal sources. Black columns represent recommended allowances of nutrients.

Minot and Murphy in 1926 [3] opened the modern era of anemia therapy when they showed that pernicious anemia could be treated successfully with whole liver. Scientists from various parts of the world began to fractionate liver in an effort to isolate the active principle which was so effective in treating persons with pernicious anemia. Eventually, refined liver extracts for parenteral administration were prepared and for the past 20 years they have been used successfully in treating thousands of persons with this disease.

In the preparation of such highly refined liver extracts nearly all the folic acid which is present in liver is lost. It occurred to me that despite the fact that folic acid is discarded early in the preparation of these extracts, it too might have antianemic properties. I knew that some of the most highly refined and concentrated liver extracts were to all intents and purposes devoid of folic acid, so it was obvious to me even before testing folic acid for special hemopoietic properties that it was not the active principle in refined liver extracts. The synthesis [4] of the structural formula as well as the chemical name of folic acid have been accepted by all groups of investigators. A new epic in nutrition and in hematology began when it was shown for the first time that persons with certain types of macrocytic anemia responded to folic acid,[5] a pure synthetic compound. The fact that persons with pernicious anemia, nutritional macrocytic anemia the macrocytic anemia of pregnancy and tropical and non-tropical sprue in relapse would respond to treatment

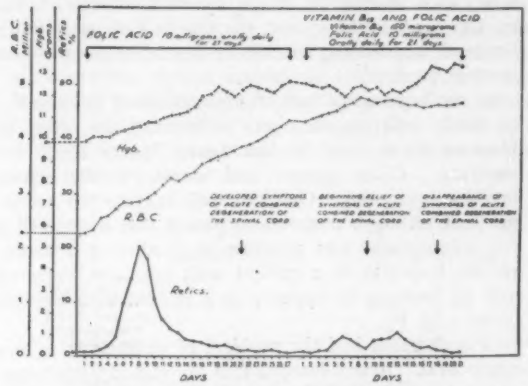
FOLIC ACID 10 milligrams orally daily for 21 days
VITAMIN B12 AND FOLIC ACID
Vitamin B12 20 micrograms
Folic Acid 10 milligrams
Orally daily for 21 days
Hgb.
R.B.C.
Retics.
DEVELOPED SYMPTOMS OF ACUTE COMBINED DEGENERATION OF THE SPINAL CORD
BEGINNING RELIEF OF SYMPTOMS OF ACUTE COMBINED DEGENERATION OF THE SPINAL CORD
DISAPPEARANCE OF SYMPTOMS OF ACUTE COMBINED DEGENERATION OF THE SPINAL CORD
DAYS
DAYS

Fig. 8.—Hemopoietic response and development of acute combined degeneration of the spinal cord on folic acid therapy in a patient with pernicious anemia; disappearance of combined degeneration of spinal cord on folic acid and vitamin B_{12} therapy.

with the pure compound indicated a closer approach to knowledge of the etiological basis and the pathogenesis of these anemias.

Soon after my associates and I demonstrated that folic acid had a beneficial effect on persons with certain types of megaloblastic anemia, we learned that it was an incomplete treatment for pernicious anemia in that neural degeneration (see fig. 8) and glossitis developed

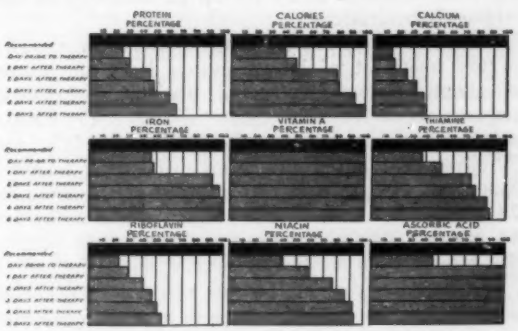

Fig. 9.—Nutrients supplied by the diet of a patient with tropical sprue before and after vitamin B_{12} therapy contrasted to the recommended allowances of nutrients.

in certain patients while they were taking it.[6] We and other investigators have shown conclusively that folic acid neither produces nor prevents these symptoms.

3. Minot, G. R., and Murphy, W. P.: Treatment of Pernicious Anemia by Special Diet, J. A. M. A. **87**: 470 (Aug. 14) 1926.

4. Angier, R. B., and others: The Structure and Synthesis of the Liver L. Casei Factor, Science **103**: 307, 1946.

5. Spies, T. D.; Vilter, C. F.; Koch, M. B., and Caldwell, M. H.: Observations on the Anti-Anemic Properties of Folic Acid, South. M. J. **38**: 707, 1945.

6. Spies, T. D., and Stone, R. E.: Some Recent Experiences with Vitamins and Vitamin Deficiencies, South. M. J. **40**: 46, 1947.

Since liver extract did prevent or relieve the symptoms of acute neural involvement so characteristic of acute combined degeneration of the spinal cord, it was obvious that it contained a nutrient as yet unknown. The search for this principle continued unabated, and independent research on both sides of the Atlantic resulted in the isolation of a red crystalline substance now called vitamin B_{12}. The Merck Laboratories, led by Dr. Karl Folkers, and the Glaxo Laboratories in England, headed by Dr. Lester Smith, made the first contributions.

In the beginning I had 46 micrograms of vitamin B_{12} to divide with my associates in Birmingham, Ala., in Havana, Cuba, and in San Juan, Puerto Rico, for studying. Other groups had similar small, almost invisible quantities. One can well imagine the excitement of testing a material so potent that a dose of a few micrograms was effective in producing a hemopoietic response in a patient with pernicious anemia and an increase in appetite in a patient with tropical sprue (fig. 9).

The chemists had the problem of characterizing this compound. It was learned that vitamin B_{12} contained about 4 per cent cobalt, that it had a molecular weight of around 1,600 and that it possessed one atom of phosphorus. Vitamin B_{12} has been converted into crystalline form by treatment with a platinum catalyst and hydrogen. Some of this material has been obtained from Dr. Karl Folkers of Merck & Company, Inc., and we have found it to be effective in producing a hemopoietic and clinical response in man. From Dr. Tom Jukes of Lederle Laboratories we obtained a crystalline compound of vitamin B_{12b}, which was isolated from Streptomyces aureofaciens. It, too, is effective in man. An identical vitamin B_{12b} product has been furnished us by Dr. A. E. Osterberg of the Abbott Laboratories.

The minimum effective parenteral dose of vitamin B_{12} in the treatment of human beings is in the range of about 1 microgram daily. The average patient requires about 100 micrograms for satisfactory remission. Exceedingly large doses—500 mg. daily for 30 days—have not produced any evidence of toxicity. More than 98 per cent was excreted in the urine in 24 hours. Ten persons had 50 micrograms a day for 18 months. Older persons often claim many subjective benefits from massive doses of vitamin B_{12}.

Before taking up the question of oral therapy with vitamin B_{12}, I would like to answer a number of questions which physicians frequently ask. Vitamin B_{12} and vitamin B_{12b} preparations derived from fermentation sources are essentially as effective per unit of weight as crystalline vitamin B_{12} preparations derived from other sources. Since the compounds are the same chemically, whether they are isolated or concentrated, there is no reason to suspect that their therapeutic effectiveness would be different. Our studies on patients to date show no demonstrable difference in activity per unit of weight for vitamin B_{12}, vitamin B_{12a} and vitamin B_{12b}. Vitamin B_{12a} and vitamin B_{12b} are identical. None of them produce toxicity when given in large amounts intramuscularly, intravenously or subcutaneously over a long period of time. Concentrates of vitamin B_{12} seem to be about as well tolerated as solutions. Untoward reactions can occur with either of them, although in our studies we have not seen such reactions. It has long been known that some patients manifest hypersensitivity to liver extracts. Some patients also are allergic to many other substances, including vitamin B_{12} and its concentrates. Many patients who are allergic to liver extract preparations, however, do not have any untoward reaction to vitamin B_{12}. Although we have not seen a patient who was allergic to vitamin B_{12} concentrates and not allergic to the crystalline form, I am sure that there are such. We see few hypersensitivity reactions because we give the material in frequent injections, which are less likely to cause an allergic condition than infrequent, haphazard periods of injections. Perhaps it is best to think of the vitamin B_{12} group of vitamins as the vitamin B_{12} complex, or a family of vitamins. This would include vitamin B_{12}, Vitamin B_{12a} (vitamin B_{12b}) and the other as yet unnamed members of the vitamin B_{12} group, or what I term the vitamin B_{12x} components.

ORAL THERAPY WITH VITAMIN B_{12}

Currently there is much interest on the part of physicians in the effectiveness of vitamin B_{12} administered orally. There are some patients with true pernicious anemia who will respond to as little as 5 or 10 micrograms of vitamin B_{12} administered orally daily. Other patients with similar clinical and hematological conditions do not respond when as much as 1 milligram is administered each day. The majority of those who respond to oral dosage will require at least 30 to 60 times the parenteral dose needed to produce a satisfactory response. The addition of the so-called intrinsic factor augments the effect of vitamin B_{12} administered orally, but one of the many preparations we have used has made the vitamin as effective orally as if the same amount were given by injection. Berk, Castle and associates have shown that normal human gastric juice contains a factor which augments the effectiveness of a heat-stable substance in beef muscle and vitamin B_{12} when administered orally.[7] Hall and his associates have repeated and confirmed these observations using Berkefeld-filtered pooled human gastric juice.[8] Bethell and his group have reported the use of an activating factor derived from hog intestines and supplied to them by the Upjohn Company.[9] Certainly, the intestines of hogs can be concentrated to produce an active component which acts as an intrinsic factor.[10] When this material is allowed to react with the proper amount of vitamin B_{12} to form a conjugate, it greatly augments the effect of the vitamin B_{12} administered by mouth,

7. Berk, L.; Castle, W. B.; Welch, A. D.; Heinle, R. W.; Anker, R., and Epstein, M.: Observations on the Etiologic Relationship of Achylia Gastrica to Pernicious Anemia: Activity of Vitamin B_{12} as Food (Extrinsic Factor), New England J. Med. **239**: 911, 1948.

8. Hall, B. F.; Morgan, E. H., and Campbell, D. C.: Oral Administration of Vitamin B_{12} in Pernicious Anemia: I. Presence of Intrinsic Factor in Berkefeld-Filtered Human Gastric Juice; Preliminary Report, Proc. Staff Meet., Mayo Clin. **24**: 99, 1949.

9. Bethell, F. H.; Swendseid, M. E.; Meyers, M. C.; Neligh, R. B., and Richards, H. G.: Observations on the Hemopoietic Factors in Hog Stomach and Duodenum, and the Treatment of Pernicious Anemia by Orally Administered Vitamin B_{12} in Combination with Extracts of Duodenal Mucosa, Univ. Hosp. Bull., Ann Arbor **15**: 49, 1949.

10. Spies, T. D.; Garcia Lopez, G.; Milanes, F.; Lopez Toca, R., and Reboredo, A.: Antianemic Properties of a Reaction Product of Vitamin B_{12} and the Intrinsic Factor, South. M. J. **43**: 206, 1950.

producing a hematological and clinical improvement in persons with pernicious anemia, nutritional macrocytic anemia and tropical sprue. Many oral preparations on the market do not contain the intrinsic factor.

To date we have not seen any oral preparation of vitamin B_{12} produce as dramatic a response as occurs when crystalline vitamin B_{12} or vitamin B_{12} concentrate is injected, or when folic acid is given orally. Recently an investigator has reported that folic acid acts as an intrinsic factor, resulting in increased effectiveness of vitamin B_{12}; the interpretation is that folic acid and vitamin B_{12} act synergistically.[11] There is no good evidence for this synergism. I have long known that either vitamin B_{12} or folic acid may be effective in the same patient, or that they may work simultaneously, but to me this does not indicate synergism and certainly does not suggest that either is the long-sought intrinsic factor.

At the moment there is no entirely practical method of oral therapy for all patients with pernicious anemia. Folic acid increases the blood values when the patient is in relapse, and sometimes the oral administration of vitamin B_{12} will produce a remission. At the present time the best method of treating the patient with pernicious anemia is the parenteral administration of liver extract or of concentrates containing vitamin B_{12}, vitamin B_{12b} and other members of the vitamin B_{12} family, or pure crystals of any of the vitamin B_{12} group derived from any source. There are only about 50,000 persons with pernicious anemia in the United States. Do not well human beings also need folic acid and vitamin B_{12} for normal health just as they need other vitamins?

SUMMARY

It should be stressed that in the history of many races there is evidence that the eating of liver was recommended to relieve illness. The modern epoch of its therapeutical use began when Minot and Murphy showed that liver is effective in producing remissions in pernicious anemia in relapse. Despite the innumerable theories that have been advanced, the pathogenesis of macrocytic anemia still is not clear. Our own studies of the effect of specific chemical substances on the cells of the bone marrow have opened a fresh and fertile field of research.

When folic acid, vitamin B_{12} or vitamin B_{12a} (vitamin B_{12b}) is administered to suitable patients intramuscularly, intravenously or subcutaneously, reticulocytosis occurs and is followed by increase in red blood cells, platelets and hemoglobin. The appetite suddenly increases, and there is a general clinical response which parallels the hemopoietic response. My associates in Cuba and I have devised a diet which in itself does not promote hemopoiesis but which, with administration of small amounts of either folic acid or any of the vitamin B_{12} family of vitamins, results in a satisfactory hemopoietic response.

I know of no disease in which there is such a variation from patient to patient and from time to time. Each patient should be evaluated and treated in the manner best for him rather than by some stereotyped rule of thumb procedure. Macrocytic anemia must be recognized as a mere symptom, and each patient must receive the form of treatment best for him. The earlier diagnosis is made, the better it is for the patient; intensive and adequate therapy should be initiated immediately. The dosage of the effective substances varies greatly from patient to patient. Irrespective of the therapeutic agent or agents used, they must be administered in excess of the quantity necessary to maintain the blood values of the patient at a normal level, as pointed out by Murphy.[12] These patients must have a diet rich in animal protein and must have all coexisting disease conditions treated. I find that frequently patients with macrocytic anemias have other stigmas of malnutrition or undernutrition. Our current method of using vitamins orally is shown in the accompanying table.

Basic Formula for Treatment with Synthetic Vitamins*

Therapeutic Agent	Daily Dose
Folic acid	5 mg.
Thiamine	10 mg.
Nicotinamide	150 mg.
Riboflavin	10 mg.
Ascorbic acid	150 mg.
† Vitamin B_{12} and "activator"	10 micrograms

* Treatment of the clinical syndromes of sprue, beriberi, pellagra, riboflavin deficiency, scurvy and certain macrocytic anemias.

† Equivalent to 10 micrograms of vitamin B_{12} and intrinsic factor adequate to form its conjugate.

There is no doubt but that there still are many precious nutrients in liver and dried (brewers') yeast powder, nutrients as yet unidentified, that may be needed in even smaller amounts than is vitamin B_{12}.

I find that after a precise and early diagnosis has been made the results of the persistent and judicious use of specific therapy are gratifying.

ABSTRACT OF DISCUSSION

DR. C. W. WIRTS JR., Philadelphia: I have had the opportunity of following six patients with what was interpreted as nontropical sprue for a period of two to four years. They had diarrhea, steatorrhea, advanced malnutrition and some anemia but no impairment of pancreatic function. Three of these patients died, and complete necropsy revealed no specific findings. To care for these patients we followed the suggestions made by Dr. Spies this morning. They were given a completely adequate diet, with an ample supply of vitamins. Crude and concentrated liver was administered orally and parenterally, and when folic acid became available it was added in daily intravenous doses as high as 200 mg. Subsequently those who survived received enormous doses of vitamin B_{12} and folic acid in the various combinations. In none of these patients was there determined a remission of symptoms which could be attributed to any specific medicament. Such improvement as was noted could be attributed to general nursing care. My question to Dr. Spies is: What is the incidence of this type of response in nontropical sprue or the spruelike syndrome? The patients that I have seen have been uniformly of this type, and their response to therapy has not been good.

DR. DWIGHT L. WILBUR, San Francisco: At the San Francisco Hospital in the last 13 years there has been a striking change in the incidence of gross deficiency diseases, and I presume many physicians have made that same observation. Thirteen years ago in one men's ward alone in the course of a winter there would be 10 to 15 cases of pellagra, usually in alcoholics. Now it is surprising if there is one. The

11. Meyer, L. M.; Sawitsky, N. D., and Krim, M.: Oral Treatment of Pernicious Anemia with Subminimal Doses of Folic Acid and Vitamin B_{12}, Am. J. Clin. Path. **20**: 454, 1950.

12. Murphy, W. P.: Anemia in Practice: Pernicious Anemia, Philadelphia, W. B. Saunders Company, 1939.

lowered incidence is due, in my opinion, not to increased knowledge of nutritional needs among those who drink alcohol but to improved economic circumstances, which permit them to buy not only more alcohol but also more food. Diseases due to insufficient amounts of protein have been somewhat neglected because of pronounced interest in vitamins in recent years. Two great unknowns face the physician when he considers nutritional problems. The first is the reason why some patients have deficiency states and others living under apparently similar conditions do not. For example, a man with carcinoma of the esophagus who goes for six months eating almost nothing will lose 40 to 50 pounds (18 to 23 Kg.) and yet not commonly show a specific vitamin deficiency. Often a well nourished patient with some other disease, who is on a deficiency diet for only a short time, will show a definite deficiency state. The second and more important question is: What will happen to the human race when for three or four generations it has been fed adequately? No one has any idea. In the last 50 years the standard rate of growth and weight of experimental animals has changed dramatically. The Oriental who lives in California and eats as Americans do has increased his weight and height so that he is considerably taller and heavier than is his counterpart in the Orient. Just how long this is going to continue, and what will be the eventual normal weight, height and rate of growth of man and woman is not known. There is something to suggest that bigness alone and rapid rate of growth alone are not desirable, because among some experimental animals, for example, resistance to certain diseases at least is not as good among animals that are well fed as it is among those who are not so well fed. Although there appears to be a definite ideal to be accomplished by adequate nutrition, there are other related problems in regard to resistance to disease, and possibly the development of degenerative diseases, which must be carefully considered.

DR. HYMAN I. GOLDSTEIN, Camden, N. J.: Aristotle recommended roast ox liver for the cure of night blindness. Hippocrates, Paul of Aegina and Celsus gave liver therapy and successfully cured night blindness. Goat liver was also used. The Babylonians and the Assyrians also knew of this (vitamin A) deficiency and the value of liver therapy. C. S. Engel of Berlin, Germany, in 1896-1898 used "sanguiniform" made from the fetal "blood-making" organs—liver, duodenum, stomach, spleen and bone marrow—and observed the rapid erythropoietic and granulocytic response.

DR. TOM D. SPIES, Birmingham, Ala.: I grew up in an area where many of my playmates and their families had pellagra. The incidence from my boyhood days until 1937 remained high. Since the advent of nicotinic acid therapy the disease in the Southern part of the United States has been eradicated, to all intents and purposes. Imagine, in the past three years working in a clinic where we see some 11,000 patients a year, we have not found a single case of pellagra. This is a fact worthy of recording. Dr. Wirts asked about the incidence of refractory cases of so-called nontropical sprue. I think that would depend on a physician's relation to the members of the profession in the rest of the community. I found in Birmingham that a certain group of physicians was sending me only patients who would not respond to anything, and as long as I dealt only in that group I had 100 per cent of such cases. If they are refractory cases, and if the doctors have given them all available forms of treatment, the physician to whom these patients are referred is going to get an equally poor result. When my associates and I began a different type of search for patients with anemia we found a great many virgin cases, so to speak; still we were not satisfied, and that is one reason why we went to study tropical sprue in Cuba. There we found about 6 per cent of the patients to be more or less the type of which Dr. Wirts spoke. Treatment may result in little benefit but not much. Most lecturers tend to talk about 94 per cent of their cases and to leave out the 6 per cent that are refractory, and I am grateful to Dr. Wirts for making the figures balance properly.

USE OF CONTROLS IN MEDICAL RESEARCH

Otho B. Ross Jr., M.D., Charlotte, N. C.

It is not surprising that laymen develop many inadequate methods of treatment for various disorders that beset the human. If an ache or pain disappears after the use of this or that remedy, it is evidence enough, to the scientifically untrained, of the efficacy of the remedy as a cure. That one event precedes another in time is the first logical step in working out a cause and effect relationship. But our untrained friends, and, frequently, trained medical scientists, stop at that stage of reasoning and experimentation. The next step is to realize that time sequence makes possible a causal connection but does not prove it. That proof is what science demands.

On reading current medical journals, one is impressed by the number of articles which extol one or another form of therapy, but which frequently lack proof of scientific merit. The great number and variety of incompletely tested treatments that are proposed as being of value, often for the same disease process, stand in bold contrast to the few which are rigidly tested according to accepted scientific criteria. It is the purpose of this study to analyze a representative group of medical articles according to one essential criterion: the use of adequate controls.

Controls are untreated patients, essential to any scientific experiment because the variable factor being measured must be compared to constants or to known variables. The course of a disease process following a form of therapy must be shown to be improved over the natural course of the disease or over other standard treatment, and in a statistically significant number of cases. This standard seems clearly necessary for an adequate evaluation, but my data indicate that it is often misused or omitted. Thus, there creep into medical literature many treatments which are quoted and requoted and finally unequivocally accepted, but which could not stand rigid scientific scrutiny.

The use of controls is, of course, an essential but preliminary step to the use of a quantitative method in experimentation. From comparison of the treated with an untreated group, the basis for statistical comparison is laid.

Mainland [1] states, "Statistical ideas, to be effective, must enter at the very beginning; i. e., in the planning of an investigation. These ideas however, lacking in so many published reports, are even less frequent in the unpublished efforts of clinicians to assess the value of their treatments. There must be something wrong with so-called scientific medical education when a young physician says that he has obtained promising results by treating [a certain syndrome with a certain agent] and yet cannot understand why a professor of pharmacology should ask about controls."

MATERIAL

The material reviewed in this article consists of 100 current articles from five leading American medical periodicals. These include: THE JOURNAL OF THE

1. Mainland, D.: Statistics in Clinical Research: Some General Principles, Ann. New York Acad. Sc. 52: 922 (March 10) 1950.

AMERICAN MEDICAL ASSOCIATION, the *American Journal of Medicine, Annals of Internal Medicine, Archives of Neurology and Psychiatry* and *American Journal of the Medical Sciences*. The articles were published between January and June of 1950 and were the first 100 to deal with some procedure or some form of therapy that was recommended or condemned. The journals were studied at random until 100 such articles were evaluated; there was no artificial selection and no exclusion. Only articles reporting a group of cases were included.

The articles were classified as: those which used adequate controls; those which used inadequate controls only; those which used no controls, and those which by nature precluded controls. A satisfactory control was defined as a number of untreated patients, or procedures, approximately equal to the number treated. These were managed in exactly the same manner as those treated, with the specific form of therapy being tested as the only variable factor. Controls that were held to be inadequate were those in which the number of untreated patients was too small, a different time or place or other variables were utilized in comparing the treated and the controls, or controls were not subjected to the same physical or emotional conditions as those treated (injections and roentgen radiation). Use of controls was held to be impossible when there were reported small numbers of unusual cases in which use of controls obviously could not have been expected or when the severity of the disease was such that none should be left untreated.

The results were as follows:

No control	45 per cent
Inadequate control	18 per cent
Well controlled	27 per cent
Control impossible	10 per cent

It is therefore seen that only 27 per cent of this sample of current recommended therapy can unquestionably be shown to improve the natural course of the disorder. Other therapy may well be beneficial, but verification of its value is not apparent in the accurate and predictable method of science. A bibliography of the articles analyzed is available on request.

ILLUSTRATIVE EXAMPLES

The following are summaries of illustrative articles demonstrating the need for adequate control:

AYMES, E. W., and PERRY, S. M.: Stellate Ganglion Block in the Treatment of Acute Cerebral Thrombosis and Embolism: Report of 44 Cases (*J. A. M. A.* **142**:15 [Jan. 7] 1950). The authors took 44 patients with cerebral thrombosis or embolism and treated them by means of cervical sympathetic block. Of the 44, 28 were stated to have shown improvement within 15 to 60 minutes. The criteria for improvement were frequently difficult to measure, and consisted of better speech, increased alertness and "improvement in behavior." No mortality rates were given for comparison with general figures or with data on an untreated group. No figures were presented to show the length of time the patients were followed or the ultimate outcome. Most important, was their improvement greater than it would have been if a stellate block had not been done?

In a disease process so variable in outcome as "stroke," in which patients show all degrees of damage between slight neurological or psychic change, to sudden death, it is difficult to evaluate any therapy except by careful comparison of groups of treated patients with controls.

The next article was done in a scholarly way from an outstanding institution, and yet without controls, in a disease that is notably variable and unpredictable:

COLLINS, H. S.; WELLS, E. B.; GOCKE, T. M., and FINLAND, M.: Treatment of Primary Atypical Pneumonia with Aureomycin (*Am. J. Med.* **8**:4 [Jan.] 1950). The authors took 40 cases of primary atypical pneumonia and found that "each showed improvement in fever and symptoms," concluding that aureomycin caused such improvement. Their work was well done, and laboratory and roentgenologic studies were accurately correlated with clinical observations, but a similar group of untreated patients was not compared. The authors state: "Definite to marked improvement occurred in every patient within the first day or two after aureomycin was started but in some instances the condition of the patient at that time was such that the improvement may have been coincidental or at least could not with any assurance be ascribed to the action of the antibiotic."

With the simple addition of a control group, such ambiguity would have been obviated. The results would be clear. If the treated patients as compared to a control group had less fever, shorter duration of illness and lower mortality or complication rate, the recommended therapy would impress even the most skeptical.

Both the above articles included data on a sufficient number of cases to be statistically important and were studies on diseases that could easily have been controlled. (In a disease such as typhoid, one would be more reluctant to withhold therapy to a control group.) In contrast to the above, the next article should be considered:

BEST, M. M.; COE, W. S.; MOORE, J. W.; REED, E. S., and CLAY, H. L.: Irradiation of the Pituitary Gland in Hypertensive Vascular Disease (*Am. J. Med. Sc.* **219**:276 [March] 1950). These investigators divided 43 hypertensive patients into two groups, into 25 treated and 18 untreated controls. All patients were placed under the x-ray machine and all thought they were actually receiving roentgen radiation; however, actual radiation was not used on the controls. The patients were then followed for symptomatic improvement and blood pressure changes; they were all evaluated in the same circumstances. Symptoms improved in 68 per cent of those actually treated, and in 77 per cent of control patients. There was no significant change in blood pressure, all readings being made under similar conditions.

A previous pituitary radiation study using no controls, which had apparently prompted the above study, had disclosed improvement. We are now able to evaluate this therapy more truly. The above article also dramatically illustrates a commonly overlooked point: the psychic element of treatment. This must always be regulated and made as constant as possible in any disease with large emotional factors.

The following report, which was possibly prompted by unjustified lay press publicity and incompletely controlled medical observations,[2] deserves study:

HOAGLAND, R. J.; DEITZ, E. N.; MYERS, P. W., and COSAND, H. E.: Antihistaminic Drugs for Colds: Evaluation Based on a Controlled Study (*J. A. M. A.* **143**:157 [May 13] 1950). The authors administered various antihistamines to 190 subjects

2. Brewster, J. M.: Antihistaminic Drugs in Therapy of Common Cold, U. S. Nav. M. Bull. **49**:1 (Jan.-Feb.) 1949.

with colds, and a large comparable control group was given placebos. Treatment was not begun until symptoms had been present for 24 hours, thus no attempt was made to evaluate very early treatment. The paper statistically and graphically shows that the number of cures or improvements were almost identical in those treated and in the controls. In this study both the patients taking and the physicians prescribing the treatment and making the examinations were unaware of what medicine was being taken. The authors state: "The widespread use of antihistaminic drugs by the public, as well as by physicians, for the cure of the common cold and the paucity of controlled work in this field require confirmatory investigations under carefully controlled conditions. . . . Any form of treatment for the common head cold is influenced by so many factors that only a rigidly controlled study eliminating as many variables as possible will provide results on which relatively valid conclusions can be based.

"There was no significant difference in the proportion of cures reported by patients receiving oral antihistaminic drugs and those receiving oral placebos. Furthermore, essentially the same proportion of patients reported no benefit from either type of treatment."

The important point of this article, it seems to me, is not its results but its method. Showing that antihistamines are not the final answer for colds is important, but doing it in carefully controlled circumstances is more so. All variables were kept as constant as possible except the one being measured.

FURTHER EXEMPLARY MATERIAL

An excellent discussion of the quantitative principles in clinical research is Reid's analysis [3] of the evaluation of streptomycin therapy of pulmonary tuberculosis by the Medical Research Council in 1948.[4] They found that, in spite of many favorable reports from the United States, there had been no well controlled evaluation of this new therapy. Reid analyzes their procedure as a model in research. After the selection of a cooperative working group of scientists, the patients were separated into treated and untreated control groups. The groups were as similar as possible and were divided completely at random. He emphasizes the random, mechanical method of separation as the only means of eliminating personal bias. He states: "A notable feature of this trial was the frank realization by all concerned of the fallibility of human judgment in general and of clinical and radiological judgment in particular. . . . All judgments were made by two or more observers, independently of each other and unbiased by any knowledge of the nature of the treatment given to the patient whose physical status was being assessed. This principle of the elimination of personal bias is fundamental in all experiment, but it is of particular importance in clinical research. Thus, in the selection of patients for inclusion in either treated or control groups, the final decision was made purely on a chance basis."

These patients were followed in a routine and standardized way, with independent observers cooperating without knowledge of the patients' identity or mode of treatment. Reid states, "The final statistical analysis by the application of the χ^2 and t tests (which conclusively demonstrated the beneficial effects of streptomycin) could thus be confidently made, since we were reasonably sure that the rain of chance events had fallen equally upon the just and the unjust. The differences observed, e. g. in case-fatality rates, between treated and control groups may be due to chance, and it is the function of the technical test of significance to test just that hypothesis. . . . Chance is always considered to be guilty or responsible for the differences until its innocence has been proved by the results of technical tests of significance. Then, and in general only then, can alternative explanations for these differences be considered. Last among these alternatives, you should consider the possibility that your own therapeutic brainchild was really producing a beneficial effect."

Such an objective approach to medical research is infrequently seen. Most experimenters have human frailties, including the desire to quickly and easily demonstrate that their pet ideas are of benefit. But we must be as skeptical of our own ideas and new treatments as we are of those of others.

COMMENT

The use of controls is frequently omitted in the evaluation of potent new therapeutic agents, such as the antibiotics. Such methods as comparison of the duration of fever in a group of treated spotted fever patients with the known duration of fever in previously reported cases are common. This type of comparison is of some usefulness, but the well known variation of virulence, of host resistance and of differences in environment, such as general care of patients, season, climate and diet, caution us to be critical. Therapeutic regimens used in diseases whose known courses are quite constant require less rigid controls for evaluation. If a new agent reduced the mortality rate of rabies from its known virtual 100 per cent to 60 per cent in a group of 10 cases, this would be of some significance even though no controls were available. However, most conditions in medicine and surgery are not so clearcut, and the more capricious they are, the more carefully we must evaluate our treatments. Again Reid states, "One must always be on the look-out for a confusion between the demonstration of a mathematical relationship and the proof of cause and effect. The association between differences in treatment and differences in outcome does not necessarily mean that the treatment has improved prognosis. The improvement may well result from some unforeseen and uncontrolled source of variation which had a selective action on one of the groups."

A recent report by Stewart Wolf [5] reemphasizes that placebos may produce observable effects which must be remembered when drug medication is instituted. Using various substances including potent drugs and placebos on a patient with a large gastric fistula through which the gastric mucous membrane could be observed, he observed "placebo effects" which can modify the actions of drugs; at times the "placebo effects" sur-

3. Reid, D.: Statistics in Clinical Research, Ann. New York Acad. Sc. **52**: 931 (March 10) 1950.

4. Streptomycin Therapy of Pulmonary Tuberculosis, Medical Research Council, Brit. M. J. **2**: 769, 1948.

5. Wolf, S.: Effects of Suggestion and Conditioning in the Action of Chemical Agents in Human Subjects: the Pharmacology of Placebos, J. Clin. Investigation **29**: 100 (Jan.) 1950.

passed the actions attributable to the drugs. He warns of the difficulty in evaluation of new drugs in patients and urges curbing of enthusiasm until the physiological effects of the placebo are taken into account.

In a recent editorial, "Are Statistics Necessary," [6] in THE JOURNAL it was stated: "If he [the investigator] is developing a new therapy, he must know how to set up fourfold tables comparing treated with untreated subjects and must know how to compute the probability that apparently favorable results were accidental."

Workers in other fields now recognize the necessity for controls. The sociologist Greenwood states,[7] "Control, we may recall, involves establishing a reliable contrast between two situations so that only the one factor under scrutiny remains free and is allowed to vary. Effective control is the key to the entire experimental procedure. It is essential for the accuracy of conclusions. Without proper control we cannot be certain that the causal nexus which we seek to establish is a real one. When an experiment has been conducted without good controls, we cannot know whether an observed effect is actually attributable to the hypothetical cause or to some other equally uncontrolled factor. We cannot tell whether the result would have been the same in the absence of any one of the factors."

It should be emphasized that the use of controls is not just a tool of highly specialized teachers or research men working with tremendous volumes of material. It is equally important to the ordinary practitioner of medicine who treats much smaller numbers of cases. Such men are at the "grass roots" of medical practice and theory and must learn to evaluate various treatments and procedures.

Although the use of comparable controls is an ideal, there are numerous instances in medicine in which small groups of unusual cases, or isolated observations, occur and will merit reporting. Observations of this type obviously cannot be as carefully controlled but frequently have definite merit. The standard outlined above must, of course, be modified or omitted in such circumstances.

SUMMARY

1. One hundred consecutive and unselected current medical journal articles describing some procedure or therapy for disease were analyzed from the standpoint of the use of controls.

2. It was found that in 45 per cent of these articles the investigators made no attempt to compare results of the specific therapy described to those in an untreated control group; 18 per cent used a control that was considered inadequate.

3. Specific examples illustrating both the presence and absence of adequate controls are cited.

4. A general discussion of the problem is presented.

5. It is suggested that a skeptical attitude be maintained toward all therapy or procedures proposed as effective unless adequate untreated parallel cases are compared. This ideal attitude must, of course, be modified when conditions prevent its adoption.

513 Professional Building.

NEOMYCIN: RESULTS OF CLINICAL USE IN TEN CASES

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and
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Neomycin, one of the newer antibiotic agents, is produced by a species of Streptomyces fradiae present in the soil. It was discovered by Waksman and Lechevalier [1] in their search for an antibiotic agent that would be effective against streptomycin-resistant strains of Mycobacterium tuberculosis. Neomycin is a basic compound readily soluble in water and most active in an alkaline medium. It is relatively thermostabile and is active against numerous gram-positive and gram-negative organisms. It is active also against streptomycin-resistant organisms; it has considerable in vitro activity against different forms of Myco. tuberculosis, in some instances showing greater activity than streptomycin. Since there is considerable tendency on the part of tubercle bacilli to develop resistance to streptomycin, the therapeutic possibilities of neomycin against clinical tuberculosis are being pursued. Waksman and his associates [2] also found that neomycin had only limited toxicity in laboratory animals and was highly effective in vivo against a variety of pathogenic organisms.

It was with the good prospect that this product would reduce further the spectrum of pathogenic bacteria unaffected by existing remedies that the present study was undertaken. Organisms naturally resistant to the antibiotic agents at hand and those which acquire a resistance during therapy and maintain this state in the present and subsequent hosts are the most important stimuli in the search for new and effective antibiotic agents.

Waksman and Lechevalier [1] emphasized that before a new antimicrobial agent can be considered to have chemotherapeutic potentialities it must be less favorable to the development of resistance among organisms and less toxic and more potent, alone or in combination with other agents, against pathogenic bacteria than

6. Are Statistics Necessary? editorial, J. A. M. A. **143**: 1260 (Aug. 5) 1950.

7. Greenwood, E.: Experimental Sociology: A Study in Method, New York, King's Crown Press, 1945.

The neomycin employed in this study was secured from Dr. G. L. Hobby, Charles Pfizer & Co., Inc., Brooklyn; Dr. L. W. Smith, the Commercial Solvents Corp., Terre Haute, Ind., and Dr. A. Gibson, Merck & Co., Inc., Rahway, N. J.

Dr. Selman A. Waksman aided this work by his counsel. The staff of the Urologic Department of the Pennsylvania Hospital, especially Drs. Leon Herman and Lloyd B. Greene, participated actively in this work, and Miss Eileen Randall gave technical assistance.

Director, Medical Divisions of the Pennsylvania Hospital and the Benjamin Franklin Clinic (Dr. Duncan); bacteriologist, Pennsylvania Hospital (Dr. Clancy); Rutgers University research associate at the Pennsylvania Hospital (Dr. Wolgamot), and assistant physician to outpatients, Pennsylvania Hospital (Dr. Beidleman).

1. Waksman, S. A., and Lechevalier, H. A.: Neomycin: A New Antibiotic Active Against Streptomycin-Resistant Bacteria, Including Tuberculosis Organisms, Science **109**: 305-307 (March 25) 1949.

2. Waksman, S. A.; Hutchison, D., and Katz, E.: Neomycin Activity upon Mycobacterium Tuberculosis and Other Mycobacteria, Am. Rev. Tuberc. **60**: 78-89 (July) 1949. Waksman and Lechevalier.[1]

available antibiotic agents. In the clinical cases reported at this time neomycin has fulfilled these criteria. A crude preparation of neomycin was employed in cases 1 and 2. Subsequent patients received the more highly purified crystalline sulfate salt, the so-called neomycin complex that was described by Swart, Hutchison and Waksman.[3] In this preliminary study the drug was used only when the pathogenic organism was insensitive, by laboratory tests, to other therapeutic agents but sensitive to neomycin. Recently in our laboratory 62 isolations of a wide variety of organisms have been found to be sensitive to neomycin but resistant, or only slightly sensitive, to other antibiotics (see the accompanying table).

METHOD

Bacterial sensitivity tests were done by a method modified from that of Bondi and co-workers,[4] in which a filter paper disk with a 2 mm. loopful of the antibiotic solution is placed on a blood agar plate which has been inoculated with the organism to be tested. The in vitro activity of penicillin, streptomycin, aureomycin, chloramphenicol and neomycin is determined on one plate. The inhibitory activity on the test organism is directly proportional to the diameter of the zone of inhibition which develops. The neomycin solution contained 200 units per milliliter and with this concentration a slightly sensitive organism showed a zone of inhibition of less than 10 mm. in diameter, one moderately sensitive a zone of 10 to 15 mm. and highly sensitive cultures a zone of 15 mm. or greater. Tube sensitivity tests were completed with 13 graded dilutions of neomycin ranging from 0.1 to 50.0 units per milliliter. Each dilution was inoculated with a broth culture of the organism to be tested, diluted 1:100, and the results were read at 24 and 48 hours. The sensitivity was recorded as the lowest concentration of neomycin which completely inhibited growth.

After several trials in evaluation, bacteriologically, of the progress in therapy for infections in the urinary tract, the following method which would indicate the number of bacteria present, even in the presence of neomycin in the urine, was adopted: three loopfuls of urine were inoculated from the edge of a blood agar plate to the center and then streaked out by the triple streak method. The urine and any drug in it are not spread far from the line of the original inoculation, but bacteria are spread beyond the drug and multiply without inhibition. A plate that remained sterile after inoculation with urine indicated the drug in the urine to be at the bactericidal level; a plate which showed growth of bacteria but a zone of inhibition along the original line of inoculation indicated a bacteriostatic level, and subcultures showing growth without inhibition indicated that the drug level was completely ineffective.

Samples of serum and urine were collected at varying times each day and assayed for neomycin concentrations. When feasible, the total urine output was measured and a neomycin assay was done. Assays of neomycin in the serum and urine were achieved by inoculation of graded serial dilutions of the fluids with a test strain of Klebsiella pneumoniae and comparison of the ensuing degree of inhibition with that obtained with the test strain in known concentrations of neomycin.

The indexes for the detection of toxic effects of neomycin were: sulfobromophthalein sodium retention, phenolsulphonphthalein test, electrocardiogram, hemogram including bone marrow, retinoscopy, audiogram and blood urea nitrogen determination. These studies were done before and after therapy, whereas multiple urinalyses were performed daily, and blood urea nitrogen and audiogram studies were done on alternate days throughout the treatment period.

3. Swart, E. A.; Hutchison, D., and Waksman, S. A.: Neomycin, Recovery and Purification, Arch. Biochem. 24: 92-103 (Nov.) 1949.

4. Bondi, A., Jr.; Spaulding, E. H.; Smith, D. E., and Dietz, C. C.: Routine Method for Rapid Determination of Susceptibility to Penicillin and Other Antibiotics, Am. J. M. Sc. 213: 221-225 (Feb.) 1947.

All urine was collected during therapy at six hour intervals for smear, culture, neomycin assay and routine urinalysis. Specimens of blood were obtained at zero, 3, 6, 12 and 24 hours after administration of the initial dose of neomycin for determination of the serum neomycin level. Thereafter determinations were done twice daily. These studies were continued through the third day following cessation of therapy.

*Data on Fifty-Four Infections with Organisms Sensitive to Neomycin and Resistant to Other Antibiotics**

Diagnosis	Organism	Neomycin	Penicillin	Streptomycin	Aureomycin	Chloramphenicol
Cystitis	A. aerogenes	S	R	R	R	Sl. S
Cystitis	A. aerogenes	S	R	R	Sl. S	R
Cystitis	A. aerogenes	S	R	R	R	R
Cystitis	A. aerogenes	S	R	R	R	Sl. S
Cystitis	A. aerogenes	MS	R	R	R	R
Cystitis	A. aerogenes	S	R	Sl. S	R	R
Cystitis	A. aerogenes	Sl. S	R	R	R	R
Cystitis	A. aerogenes	MS	R	R	R	R
Cystitis	A. aerogenes	Sl. S	R	R	R	R
Cystitis	A. aerogenes	S	R	R	R	R
Cystitis	A. aerogenes	S	R	R	R	Sl. S
Cystitis	A. aerogenes	MS	R	R	R	Sl. S
Cystitis	A. aerogenes	S	R	R	Sl. S	MS
Cystitis	Geotrichum	S	R	R	R	R
Cystitis	Ps. aeruginosa	S	R	Sl. S	R	R
Cystitis	Ps. aerugnosa	Sl. S	R	R	R	R
Cystitis	Ps. aeruginosa	MS	R	R	R	R
Cystitis	Ps. aeruginosa	MS	R	R	R	R
Cystitis	Ps. aeruginosa	S	R	Sl. S	R	R
Cystitis	A. aerogenes	S	R	R	R	R
Cystitis	A. aerogenes	S	R	R	Sl. S	R
Cystitis	Proteus	MS	R	R	R	R
Cystitis	Hem. Staph. aureus	S	R	R	R	R
Cystitis	Hem. Staph. aureus	Sl. S	R	R	R	R
Cystitis	Hem. Staph. aureus	MS	R	R	R	R
Cystitis	Hem. Staph. aureus	S	R	R	R	R
Cystitis	Staph. albus	S	R	Sl. S	Sl. S	Sl. S
Cystitis	Staph. albus	Sl. S	R	R	R	R
Cystitis	Pseudomonas	MS	R	R	R	R
Cystitis-prostatitis	Pseudomonas	Sl. S	R	R	R	R
Cystitis-prostatitis	Staph. albus	MS	R	R	R	Sl. S
Cystitis-prostatitis	Coliform bacillus	MS	R	R	R	Sl. S
Cystitis	Coliform bacillus	MS	R	R	R	R
Cystitis	Coliform bacillus	S	R	R	R	R
Cystitis	Aerogenes-like	MS	R	R	R	R
Cystitis	Gram-neg. Rod	MS	R	R	R	R
Cystitis	Esch. coli	Sl. S	R	R	R	R
Pyelonephritis	Esch. coli	MS	R	R	R	R
Pyelonephritis	Esch. coli	MS	R	Sl. S	R	Sl. S
Pyelonephritis	Pseudomonas	S	..	R	R	R
Pyelonephritis	Pseudomonas	S	..	R	R	R
Pyelonephritis	A. aerogenes	S	R	R	R	R
Pyelonephritis	A. aerogenes	S	R	R	R	Sl. S
Pyelonephritis	A. aerogenes	S	..	R	R	Sl. S
Hematuria	Esch. coli	MS	R	Sl. S	R	R
Prostatitis	Esch. coli	S	R	Sl. S	R	R
Vesicovaginal fistula	Pseudomonas	Sl. S	R	R	R	R
Pneumonia	Hem. Staph. aureus	S	R	R	R	R
Pneumonia	Hem. Staph. aureus	S	R	R	R	Sl. S
Pneumonia	Pseudomonas	Sl. S	R	R	R	R
Pneumonia	K. pneumoniae	MS	R	R	R	R
Wound infection	Esch. coli	S	R	R	R	R
Wound infection	Coliform bacillus	Sl. S	R	R	R	R
Wound infection	Staph. aureus	S	R	MS	R	R
Wound infection	Staph. albus	MS	R	R	R	R
Appendical abscess	Coliform bacillus	Sl. S	R	R	R	R
Appendical abscess	Coliform bacillus	MS	R	R	R	R
Peritonitis	Pseudomonas	Sl. S	R	R	R	R
Pyodermia	Hem. Staph. aureus	S	R	Sl. S	Sl. S	Sl. S
Cellulitis of hand	Hem. Staph. aureus	MS	R	R	R	R
Cellulitis of foot	Esch. coli	MS	R	R	R	Sl. S
Abscess of foot	Coliform bacillus	Sl. S	R	R	R	R

* These 62 isolations of various organisms, sensitive by disk test to neomycin but resistant—completely or moderately so—to aureomycin, penicillin, streptomycin and chloramphenicol, were so classified in 475 consecutive sensitivity tests performed in our laboratory. The clinical condition with which each was associated is recorded. The letter S denotes sensitive; MS, moderately sensitive; Sl. S, slightly sensitive, and R, resistant.

REPORT OF CASES

CASE 1.—*Pyelonephritis and Bacteremia.*—R. P., a man aged 47, was admitted as a patient of the Benjamin Franklin Clinic on Aug. 13, 1949. He was known to have had bilateral pyelonephritis for three and one-half years. Previous treatments with penicillin, aureomycin, chloramphenicol and urinary antiseptics were given at different times. A transient improvement followed each course, but subsequent respective therapies were without effect.

The patient was acutely ill and moderately obese; the liver was enlarged, and tenderness over the left renal area was acute. Pyuria was present, and an abundant growth of Aerobactor aerogenes was cultured from the urine. Roentgenologic studies showed an enlarged left kidney with an irregular outline. Both ureters were large and atonic, as in long-standing infections of the urinary tract. A differential phenolsulphonphthalein test revealed good function in each kidney. After a severe chill the body temperature rose to 105 F., and on August 19 A. aerogenes were isolated from the blood and found to be completely resistant to streptomycin, aureomycin, chloramphenicol and penicillin. Furthermore, no benefit accrued from combined penicillin and streptomycin therapy.

On August 31, after a period of critical illness, the fever subsided and the patient's condition was improved but pain and decided tenderness in the region of the left kidney persisted. A culture of the blood was negative, but the degree of pyuria was unchanged and an abundant growth of A. aerogenes on culture of the urine persisted.

A crude preparation of neomycin containing 200 units per milligram was secured for us by Dr. Waksman. The pyrogen content of the drug was not known, nor was the preparation known to be sterile. The drug was prepared for intramuscular injection by pasteurization after its solution in normal saline. The organism A. aerogenes was sensitive to less than 1 unit per milliliter. The patient had no toxic manifestations after injection of the initial dose of 20,000 units of neomycin, which was followed in four hours by 40,000 units and thereafter 80,000 units every fourth hour for four doses. The patient received 380,000 units in the first 24 hours and thereafter for four days 400,000 units in four divided doses per 24 hours—a total of 1,980,000 units.

A culture was taken of each urine specimen voided after the institution of neomycin therapy. The first specimen, four hours after the initial injection, yielded a heavy growth of A. aerogenes, the second specimen at 8 hours a scant growth. Subsequent cultures were negative, including one taken each week after discharge up to and including Dec. 27, 1949. Neomycin assay of the urine revealed concentrations of 15 to 30 units per milliliter.

The pyuria promptly subsided, although rare plus cells were present in the urine when the patient was discharged on Sept. 8, 1949. Furthermore, the patient became free from symptoms and this state was maintained as of December 27. Beyond some discomfort at the site of injection, which was not greater than that when streptomycin was injected, there were no untoward effects.

CASE 2.—*Prostatism, Uremia and Pyelonephritis.*—A. J., a man aged 64, was critically ill when admitted Aug. 30, 1949. He had profound acidosis, with the carbon dioxide-combining power 4.5 milliequivalents per liter (10 volumes per cent) and a blood urea nitrogen level of 240 mg. per 100 cc., secondary to prostatism. After gradual decompression of his bladder the blood urea nitrogen level decreased to 35 mg. per 100 cc. and the acidosis subsided, but a urinary tract infection with A. aerogenes persisted. A scant growth of Pseudomonas aeruginosa (B. pyocyaneus) and later a fungus believed to be Geotrichum was recovered from the urine. The A. aerogenes was sensitive to neomycin and moderately sensitive to chloramphenicol. The Ps. aeruginosa was exceedingly sensitive and the Geotrichum was moderately sensitive to neomycin, but each was resistant to the other antibiotic agents.

The neomycin therapy was identical with that employed in the first case. The urine was sterile within 12 hours after the first injection, but on the second and third days of treatment only six sterile specimens were obtained, six others being grossly contaminated with Ps. aeruginosa and the fungus. On the morning of the fourth day the urine was sterile, and it remained so for the duration of three days of therapy. A specimen on the following day was sterile, but as a retention catheter was still in place it was not surprising that the urine became contaminated with a paracolon bacillus several days later. A two stage prostatectomy was completed on Oct. 27, 1949, and the patient was discharged on November 12. No toxic effect of the drug was noted.

CASE 3.—*Pyelonephritis and Pneumonitis.*—S. V., a baker aged 54, was seen on the urology service in March 1949. A nephrolithotomy done elsewhere six months previously was followed by pain in the right flank and by pyuria. The renal function was poor bilaterally, and cultures of the urine revealed hemolytic Escherichia coli. The pyuria responded to a course of sulfadiazine but recurred with acute symptoms in November 1949, at which time the man was readmitted to the hospital. An abundant growth of hemolytic Esch. coli was recovered on culture of the urine. A transitory fever subsided, and the urine became sterile on treatment with penicillin on one occasion and with gantrisin® (3,4-dimethyl-5-sulfanilamidoisoxazole) plus streptomycin on another. After each course of therapy the hemolytic Esch. coli returned. The bacilluria recurred during penicillin therapy for the intercurrent pneumonitis. The Esch. coli organism was resistant to streptomycin, aureomycin and chloramphenicol. The crystalline sulfate salt of neomycin, to which the organism was sensitive, was administered (100,000 units intramuscularly every six hours) from Dec. 22 to 29,

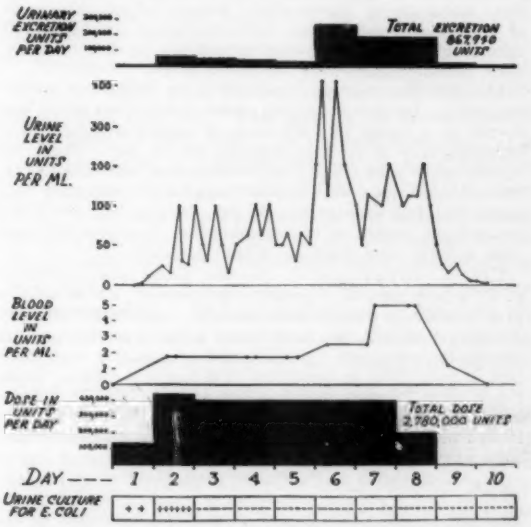

Chart (case 3, S. V.) illustrating urinary excretion, urine levels and blood (serum) levels of neomycin, and urine culture studies in relation to the intramuscular dosage of neomycin. In this case neomycin therapy was discontinued after 7½ days. Comparable curves were obtained in cases 4, 6, 8, 9 and 10.

1949. The urine was sterile 36 hours after the patient received the first dose and remained so except for the transient appearance of an Enterococcus which was resistant to neomycin but responded promptly to gantrisin® therapy. The patient remained afebrile and asymptomatic, and no untoward effects from neomycin therapy were noted. Urinalysis on March 4, 1950 revealed no red or white blood cells, and the specimen was sterile. Serum and urine neomycin values per milliliter in relation to therapy are presented, and the effectiveness of therapy is indicated in the accompanying chart.

CASE 4.—*Cystitis, Hypertrophy of Prostate Gland and Prostatitis.*—J. L., a man aged 62, a Spanish-American who was a cigar maker, had increased urinary frequency and urgency, dysuria, nocturia, suprapubic and perineal pain after a transurethral prostatectomy in 1947. Treatment with sulfadiazine, penicillin and streptomycin was ineffective. When hospitalized on Jan. 4, 1950 he was voiding every 15 to 20 minutes during

the day and eight to 10 times at night. He was malnourished, had suprapubic tenderness and grade 2 prostatic hypertrophy with pronounced tenderness over the prostate gland. The urinalysis revealed a 1 plus reaction for albumin, an occasional red blood cell and pus. Cystoscopy disclosed a contracted bladder with partial obstruction at the site of the previous incomplete prostatectomy. A culture of the urine produced A. aerogenes which was sensitive only to neomycin. A solution of neomycin sulfate, 100,000 units, was given intramuscularly every six hours for six days. The urine became sterile within four hours after the patient received the first dose and remained so. No untoward effects of therapy appeared. A transurethral resection of the prostate was performed on Jan. 29, 1950. The postoperative course was uneventful, and the patient was discharged symptom free on January 28.

CASE 5.—*Paracolon Bacillus, Bacteremia and Pyelonephritis.*—J. J., an infant 19 days of age, was admitted to Dr. John P. Scott's service at the Children's Hospital of Philadelphia on Nov. 25, 1949 because of weight loss, vomiting, fever, diarrhea, intense jaundice and enlarged liver appearing serially during the preceding week. Studies revealed leukocytosis and polynucleosis, 3 plus cephalin flocculation liver function test, gamma globulin 0.8 Gm. per 100 cc., and serum bilirubin 19 mg. per 100 cc. total with 10.8 mg. of the prompt reacting bilirubin. Pyuria was present, and a culture of the urine revealed paracolon bacilli. When the infant received supportive treatment including fluids intravenously, plasma, multiple whole blood transfusions and streptomycin parenterally, there was moderate improvement. Despite subsequent courses of aureomycin, sulfadiazine, chloramphenicol and gantrisin® cultures of the urine remained persistently positive for paracolon bacilli.

The offending organism was found to be sensitive to neomycin, and on January 8 the 8½ pound (3,856 Gm.) infant was started on a dosage of 4,498 units of neomycin sulfate given intramuscularly at six hour intervals for six days. The urine became sterile after the first day of treatment and remained so. No untoward local or systemic response of neomycin was noted, and follow-up studies on Jan. 19 and Feb. 20, 1950, revealed the patient to be asymptomatic. The urinalysis and urine cultures were negative on both occasions.

CASE 6.—*Hypertrophy of Prostate Gland and Cystitis.*—E. Z., a man aged 48, married, a store-keeper, had a nephropexy in 1923, a transurethral prostatic resection followed by a urinary tract infection in 1934 and a partial resection of the bladder for carcinoma, again followed by a urinary tract infection, in July 1949. In September 1949 he noted dysuria, "dark, cloudy urine," frequency of urination and nocturia. In November 1949 a mass was detected in the cystectomy scar and was treated with roentgen radiation. However, his symptoms, with some nausea, became progressively more severe.

On his admission to the Pennsylvania Hospital on Jan. 25, 1950 he had a nodular extravesicular mass in the left lower quadrant of the abdomen and generalized tenderness in the suprapubic region. There was a 2 plus reaction for albuminuria, and there was decided pyuria. The blood urea nitrogen level was 38 mg. per 100 cc., and a hemogram, a roentgenogram of the abdomen and a cystometrogram were normal; there was no cystoscopic evidence of carcinoma. An abundant growth of coliform bacilli which were exceedingly sensitive to neomycin, moderately sensitive to chloramphenicol and resistant to penicillin, streptomycin, and aureomycin was cultured from the urine. Also, there was an abundant growth of Ps. aeruginosa which was moderately sensitive to neomycin but resistant to penicillin, streptomycin, chloramphenicol and aureomycin.

After the cystoscopic examination of the patient on Feb. 2, 1950 there developed chills, high fever, nausea and headaches. Gantrisin® therapy aggravated the nausea and produced vomiting with no apparent clinical benefit, and treatment with procaine penicillin, 300,000 units daily, had no apparent effect. A second urine culture confirmed the previous results. Neomycin sulfate therapy was begun on February 7, the fifth day of fever, 45,700 units being given intramuscularly every six hours. The fever abated but the patient complained of increasing nausea and vomiting. Also, the blood urea nitrogen concentration had risen from 41 to 85 mg. per 100 cc., and his hearing had become considerably impaired as indicated by audiogram studies. Cultures of the urine showed that the coliform bacillus had been eradicated after the first dose of neomycin but that Ps. aeruginosa had persisted.

Neomycin therapy was stopped after 72 hours (13 doses totaling 982,550 units). The nausea and vomiting subsided, and the patient's hearing improved about 50 per cent as measured by audiogram studies. The blood urea nitrogen value was still elevated (75 mg. per 100 cc.) on March 1. Repeated cultures of the urine revealed only Ps. aeruginosa.

CASE 7.—*Acute Bacterial Endocarditis, Pneumonia and Pyelonephritis.*—L. M., a Negro housewife aged 63, entered the hospital on Feb. 7, 1950 with a history of headache, chills and fever of 24 hours' duration and delirium of eight hours' duration. She had fever (105 F.), tachycardia, hyperpnea, nuchal rigidity, delirium and signs of consolidation over the lower lobe of the right lung. Results of studies of the spinal fluid and hydrodynamics were normal, as were routine urinalysis and blood count. Intensive antibiotic therapy was begun after blood, urine and spinal fluid were taken for culture. Penicillin, streptomycin and aureomycin were given. Hemolytic Staphylococcus aureus, completely resistant to penicillin but sensitive to aureomycin, streptomycin, chloramphenicol and neomycin, was recovered from cultures of the blood, urine and sputum. Accordingly, penicillin therapy was stopped; streptomycin, 2 Gm., was given intramuscularly and aureomycin 400 mg. intravenously daily, was continued. A second lumbar puncture showed only 40 neutrophils and 10 lymphocytes with negative Wassermann reaction and culture. Intravenous administration of fluids and feeding by gavage were employed. The body temperature fluctuated from 103 to 104 F., and the patient remained comatose with changing neurological abnormalities. Neomycin sulfate, 185,000 units intramuscularly in four equal doses six hours apart, was given daily after the fifth hospital day but the patient's condition remained unchanged. A blood culture 24 hours after the start of neomycin therapy was still positive but was negative on each of two succeeding days. A culture of the spinal fluid at this time was again negative; the spinal fluid demonstrated no antibiotic activity against an organism sensitive to each of the drugs being administered. The white blood cell count gradually rose to 19,600 per cubic millimeter, the blood urea nitrogen value remained at 20 to 25 mg. per 100 cc., and urinalysis revealed pyuria and the hemolytic Staph. aureus as the only abnormalities.

The patient's condition gradually deteriorated, and respirations ceased on the tenth hospital day. Autopsy revealed an acute ulcerating bacterial endocarditis of the mitral valve, pneumonia of the right lower lobe, acute pericarditis, an epicardial abscess and edema and congestion of the brain. Although the illness ended fatally it appears significant that the peripheral blood became sterile only after neomycin was administered. Also, there was no discernible antibiotic activity in the spinal fluid. No recognizable toxic effects of neomycin therapy could be identified in any of the organs.

CASE 8.—*Bladder Calculus and Bacterial Cystitis.*—A. P., a man aged 53, a detective, in January 1949 was treated surgically at another hospital for a brain abscess. He had permanent residual loss of memory, blurring of vision, partial deafness and ataxia. In December 1949 he noted progressive dysuria, nocturia and frequency of urination. On Feb. 9, 1950 he was admitted to the urologic service at the Pennsylvania Hospital. He was afebrile and not in acute distress, but he had a moderately enlarged prostate. Roentgenologic and cystoscopic examination revealed a large calculus in the bladder. A cystometrogram was normal. The urine was normal except for many red and white blood cells. Cultures of the urine on February 10 and 15 revealed abundant coliform bacilli which were decidedly sensitive to neomycin but resistant to penicillin, streptomycin, chloramphenicol and aureomycin.

On the fifth hospital day a suprapubic cystotomy was done, the calculus removed and suprapubic and urethral catheters left in place. On the first postoperative day, the patient had tachycardia and fever. Neomycin sulfate therapy, 45,700 units given intramuscularly every six hours, was started. The first urine specimen, collected from the fourth to the eighth hour thereafter, was sterile, and succeeding cultures remained so. The temperature and pulse rate returned to normal within

48 hours. Routine urinalyses, however, continued to reveal many red and white blood cells; the suprapubic and urethral catheters were in situ.

Neomycin therapy was stopped after 54 hours, without the return of fever or bacilluria. Studies for evidences of toxic effects of neomycin revealed no significant changes. A transurethral resection of the prostate gland was performed on February 23. The postoperative course was uneventful, and the patient left the hospital on March 3. At the time of his discharge, he was able to void freely without discomfort and the urine was grossly clear.

CASE 9.—*Renal Calculi and Pyelonephritis.*—M. M., a man aged 46, was admitted to the urologic service for the seventh time on March 11, 1950, with complaints of chills, fever, malaise and burning pain in the left flank. He had experienced similar episodes, attributed to bilateral pyelonephritis, intermittently for the past 20 years. Nonhemolytic streptococci and Pseudomonas organisms had been cultured from the urine on his first admission in 1941. Over the years he had been treated with sulfathiazole, sulfadiazine, penicillin, streptomycin and aureomycin in adequate dosages without lasting benefit. On this admission he was acutely ill with a temperature of 104.2 F. There was deep tenderness in the left lower quadrant of his abdomen and in the flank. Severe pyuria was constantly present, but the urine was otherwise normal. Cystoscopy revealed no abnormalities, but retrograde pyelography demonstrated, for the first time, two small calculi in the left kidney. Culture of urine from the left ureter yielded abundant Proteus and nonhemolytic streptococci which required 30 units of neomycin per milliliter to inhibit growth and were completely resistant to all other antibiotics. Culture of urine from the right ureter yielded abundant Pseudomonas organisms insensitive to all antibiotics, including neomycin.

With supportive therapy only, fever and subjective symptoms abated within 48 hours. Despite in vitro evidence of pronounced resistance to neomycin of all three infecting organisms, it was believed—in view of previous failures with other antibiotics—that a course of neomyycin therapy was warranted. Neomycin sulfate therapy, 50,000 units intramuscularly every six hours for the first day and every 12 hours thereafter, was instituted on March 11. Immediately afterward the Proteus organism disappeared from the urine cultures. However, the Streptococcus and Pseudomonas continued to appear in undiminished numbers. Because of failure to attain satisfactory neomycin levels in the urine the dose was increased on March 14 to 100,000 units every 12 hours and on March 17 to 100,000 units every six hours. On March 20 neomycin therapy was stopped after a total of 2,100,000 units had been given. The pyuria was undiminished and Pseudomonas and nonhemolytic streptococci were still present on smear and culture of the urine. The maximum blood level attained was 5 units per milliliter of serum on the fourth day of treatment, and the maximum urine level achieved was 128 units of neomycin per milliliter on the last day of treatment.

No indications of toxic effects of neomycin were detected. Save for obliteration of the Proteus from the urine cultures, the antibiotic therapy must be considered a failure in this case. Conceivably the initial dosage was too small and the interval between injections too long. No evidence of increasing resistance of the infecting organisms to neomycin was noted in vitro.

CASE 10.—*Bacterial Cystitis.*—M. M., a woman aged 61 with hypertensive cardiovascular disease and hemiplegia was hospitalized on Jan. 31, 1950. The spinal fluid was grossly bloody, and her clinical course and rehabilitation were otherwise consistent with a diagnosis of cerebral hemorrhage. Because of incontinence of urine an indwelling catheter was employed. From February 5 until March 5 she received sulfadiazine, 0.5 Gm. twice daily, as a prophylaxis against infection of the urinary tract, but on February 26 there developed fever (103 F.) without localizing physical signs. The fever continued, and on March 1 there was severe pyuria; culture of the urine yielded abundant A. aerogenes organisms which were moderately sensitive to neomycin and chloramphenicol but resistant to all other antibiotics. Penicillin and gantrisin® in therapeutic doses were without apparent effect on the fever or pyuria.

On March 18 neomycin sulfate therapy, 100,000 units intramuscularly every six hours for four doses and every 12 hours thereafter, was begun. On March 21 the dose was reduced to 50,000 units every 12 hours until cessation of therapy on March 22, after a total dosage of 950,000 units had been given. The first urine culture taken six hours after the initial injection of neomycin sulfate solution yielded no growth, nor did 11 subsequent cultures. The pyuria had abated completely when therapy was terminated.

In this instance a dose of neomycin at 12 hour intervals was eminently satisfactory. Neomycin blood levels determined twice daily ranged from 4 to 8 units per milliliter of serum, and urine levels noted four times daily ranged between 102 and 410 units per milliliter. As judged by pretreatment and posttreatment toxicity detection studies, there were no apparent adverse systemic or local effects of neomycin.

SUMMARY AND CONCLUSION

It has been shown that a wide variety of pathogenic organisms insensitive to antibiotics in current use were sensitive to neomycin in vitro. Ten cases in which neomycin therapy was employed are reported. Each patient had a bacterial infection due to one or more pathogenic organisms which were completely or moderately resistant to penicillin, aureomycin, chloramphenicol and streptomycin, while all but one—a Pseudomonas—were known to be sensitive to neomycin.

Neomycin was given intramuscularly, in doses varying from 4,498 units (to an infant) to 100,000 units at six hour intervals. The duration of therapy varied from three to nine days. In the infections due to a sensitive organism, 100,000 units at six hour intervals for four doses and thereafter 50,000 to 100,000 units at 12 hour intervals for five to seven days ordinarily appeared adequate, but dosage required regulation in accord with the desired blood and urine concentrations of neomycin, which in turn are related to the sensitivity of the organism. The concentrations of neomycin in the serum and urine were built up gradually, usually reaching a maximum after 48 to 72 hours of therapy. After adequate therapeutic levels had been achieved, the serum and urine levels remained relatively stable on either a six or 12 hour dosage schedule. The maximum serum levels varied from 4 to 10 units per milliliter, but in patients with poor renal function rapidly built up to and in excess of 16 units. Maximum urine levels varied from 26 to 410 units per milliliter. Measurable quantities of the drug persisted in the serum for 24 to 36 hours after cessation of therapy, while urinary excretion continued in declining amounts for 48 to 72 hours after treatment had ceased.

Neomycin was dramatically effective in eradicating organisms sensitive to it from the blood and urinary tract. It is considered significant that in no case in which the sensitive organism was eradicated did it return after cessation of therapy. The original observations of Waksman and Lechevalier [1] on the bactericidal properties of the drug were confirmed. However, most strains of Proteus, and more especially the Pseudomonas cultures, exhibited properties suggesting potential development of resistance to neomycin. For example, a strain of Pseudomonas which was presumably sensitive to 4 units of neomycin after 24 hours' incubation revealed growth in a concentration of 20 units of neomycin per milliliter at 48 hours; after 8 days'

incubation there was even growth in the tube containing 100 units of neomycin per milliliter. This potentiality necessitates administration of the drug in dosage sufficient to attain serum and urine concentrations in excess of those indicated as efficient by the in vitro tests.

Apparent evidences of toxicity were confined to one patient and consisted of impaired hearing and an increased blood urea nitrogen level. Improved hearing followed cessation of therapy, but elevation of the blood urea nitrogen values persisted. Although proof of a direct relationship between neomycin therapy and these changes is lacking, it is believed that treatment with the drug should be discontinued in any patient manifesting impaired hearing or urea nitrogen retention while receiving neomycin.

It is concluded that neomycin is an extremely effective agent in the treatment of clinical infections, particularly those of the urinary tract. Clinical evaluation of neomycin in the treatment of tuberculosis is in progress and will be the subject of a future report.

GEOGRAPHIC BLOOD GROUP VARIABILITY IN THE UNITED STATES

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To present information concerning geographic variability of the ABO blood group distributions, some facts learned from the records of the National Blood Program are discussed in this paper. Chosen for review are the data pertaining to 141,774 white persons who voluntarily contributed blood to the American Red Cross in 15 cities and 637 outlying communities during the period January 1948 through March 1949. This is one of the largest aggregate samples ever described for a program under standardized technical procedures.

The majority of the blood donors consisted of persons in the industrial, clerical and professional classes. Although the 15 regional samples of employed white persons were selected without regard to their meeting statistical requirements, there is adequate reason to believe that the criterion of randomness was satisfied in very appreciable degree. Men predominated numerically, ranging from 65 per cent in Springfield, Mo., to more than 80 per cent in Charlotte, N. C., and Detroit. No significant difference in the incidence of any blood group could be determined between men and women; consequently, the assembled material was combined for the two sexes.

For the regions as a whole, the blood group percentages and corresponding standard deviations can be stated as follows: O, 45.55 ±0.13; A, 40.77 ± 0.13; B, 9.96 ± 0.08, and AB, 3.72 ± 0.05. These over-all percentages differ in minor degree from those previously reported by Snyder,[1] based on 20,000 persons in the United States. The constituent distributions, arranged from north to south, are set forth in the table.

Since the data were all procured in the same period and are broken down geographically, detailed comparisons with proportions stated in the blood group literature would be impracticable. As a matter of record, the fact should be mentioned that a distribution given by Schiff [2] for a Berlin sample of 39,174 persons is within the ranges of the figures in the lower section of the table. Also, similarities are detectable in the percentages relating both to the Royal Air Forces and to the City of Cambridge, England (sample, 199,221), published by Dobson and Ikin [3]; to Paris (1,265), by Dujarric de la Rivière,[2] and Glasgow (only 746), by Matta.[2] Few references deal with large numbers of individuals.

Sample Blood Group Distributions of White Persons, by Regions

Number of Persons in Each Blood Group

Region *	O	A	B	AB	Total
Yakima, Wash.	736	706	148	66	1,656
Rochester, N. Y.	10,562	9,987	2,394	894	23,787
Detroit	2,396	2,350	683	299	5,728
Massachusetts	10,810	9,993	2,405	794	23,332
Omaha	2,285	2,182	592	215	5,274
Columbus, Ohio	2,585	2,535	539	210	5,869
Washington, D. C.	7,043	6,239	1,568	569	15,419
St. Louis	3,044	2,856	654	276	6,830
Stockton, Calif.	2,680	2,397	582	223	5,892
Wichita, Kan.	3,084	2,741	601	280	6,656
San Jose, Calif.	2,109	1,737	405	143	4,394
Springfield, Mo.	1,715	1,522	339	115	3,691
Charlotte, N. C.	2,392	2,079	451	158	5,080
Los Angeles	7,286	6,452	1,579	621	16,088
Atlanta, Ga.	5,804	4,811	1,115	398	12,128
All regions	64,581	57,807	14,115	5,271	141,774

Percentage in Each Group

Yakima, Wash.	44.44	42.63	8.94	3.99	100
Rochester, N. Y.	44.40	41.78	10.06	3.76	100
Detroit	41.83	41.03	11.92	5.22	100
Massachusetts	46.33	39.70	10.57	3.40	100
Omaha	43.33	41.37	11.22	4.08	100
Columbus, Ohio	44.04	43.19	9.19	3.58	100
Washington, D. C.	45.68	40.46	10.17	3.69	100
St. Louis	44.57	41.82	9.57	4.04	100
Stockton, Calif.	45.49	40.68	9.88	3.95	100
Wichita, Kan.	45.58	41.18	9.03	4.21	100
San Jose, Calif.	48.00	39.53	9.22	3.25	100
Springfield, Mo.	46.46	41.24	9.18	3.12	100
Charlotte, N. C.	47.09	40.92	8.88	3.11	100
Los Angeles	46.05	40.23	9.85	3.87	100
Atlanta, Ga.	47.86	39.67	9.19	3.28	100
All regions	45.55	40.77	9.96	3.72	100

* The latitude of each city listed, which for analytical purposes was assumed to be representative of the region, can be found in any atlas. For Massachusetts 42.3 degrees north was considered typical.

Comparison of the intracolumn percentages in the table, two at a time, reveals 164 cases in which the differences were at least twice their standard errors. Thus the sample data indicate that 6.2 individuals more per 100 belonged to the O group in the San Jose population than in the Detroit population. The statistically meaningful differences appear often enough to warrant the following condensation:

1. O varied inversely with either A or B and directly with AB (R=0.74±0.12).

From the National Blood Program, the American National Red Cross.

1. Snyder, L. H.: Blood Grouping in Relation to Clinical and Legal Medicine, Baltimore, Williams & Wilkins Company, 1929.
2. Cited by Boyd, W. C.: Blood Groups, Tabulae biol. **17**: 113-240, 1939.
3. Dobson, A. M., and Ikin, E. W.: The ABO Blood Groups in the United Kingdom: Frequencies Based on a Very Large Sample, J. Path. & Bact. **58**: 221-227, 1946.

2. A varied inversely with either O or B and directly with AB ($R=0.69\pm0.14$).

3. B varied inversely with either O or A and directly with AB ($R=0.87\pm0.06$).

4. The corresponding AB correlation fell short of being significant ($R=0.41\pm0.21$).

More than anything else, the above facts focus attention on the unique status of AB. Whereas the variability of O, A or B is measurable in part by that of AB, evidence of the reverse is lacking. From region to region the greater the O, A or B percentage, the smaller on the average was the percentage for the remaining groups within the trio, but AB tended to be stable. Pertaining to a single period, the multiple relationships, of course, fail to yield information of a dynamic character. Only through study of sequential data will it be feasible to evaluate the extent that the phenotypes O, A and B are mutually competitive and just how changes in their relative frequencies affect the occurrence of AB.

Information was sought concerning the directional nature of the geographic variability, and again AB was found to contrast with the other groups. In terms of degrees latitude three relationships were determined, two rather pronounced (O, B) and the third moderate (A). The AB correlation was without significance ($r = 0.40 \pm 0.22$). No east-west trends were discovered.

For each degree of latitude proceeding from north to south the O percentage was greater by 0.32 on the average. To explain this tendency on the ground of adaptive variability, as understood in the genetic sense, would be unjustifiable. Probably the most acceptable interpretation is that in the South the hereditary lines of the early settlers, many of whom were Scotch, Irish, and Welsh in origin, have been subjected to less admixture from the outside than in the North. In the southwestern regions the ancestry of some persons recorded as white may be partly American Indian, slightly raising the O percentages therein. The correlation ($r = 0.66 \pm 0.14$) would have been stronger if the Massachusetts sample had not been aberrant by virtue of an exceptionally large proportion of O individuals.

From north to south the B percentage averaged 0.17 smaller per degree of latitude. Here too one notable deviation weakened the correlation ($r = 0.62 \pm 0.19$), as the sample for Yakima, the most northern region, contained the fewest relative number of B individuals; even with the inclusion of 1,100 supplementary cases the Bs constituted less than one tenth of the Yakima total. The A relationship, though significant ($r = 0.51 \pm 0.19$), is deemed of little importance quantitatively.

SUMMARY

A review of sample data collected in 15 regions discloses variability somewhat strong in reference to groups O and B, moderate for A, and, except in occasional instances, lacking in reference to AB. As a statistical measure of directional variability, degrees of latitude were applied with partial success. Some additional criterion remains to be discovered before geographic formulas will be utilizable for the satisfactory estimation of the incidence of any group in a specific region. Nevertheless, in the event of an emergency requiring large quantities of blood, the southern areas now appear to be comparatively favorable sources of O and the northern areas of B. In the United States the respective proportions for white persons seem to have achieved a distinctiveness that is regional, not national, in character. Still to be answered is the question: Will the observed conditions remain static? Population changes could be responsible for marked changes within the span of a very few years.

LIMITATIONS OF ROENTGEN RAYS IN DIAGNOSIS OF BLADDER STONE

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and
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This study was undertaken to determine the frequency with which roentgenograms failed to show the presence of bladder stones. It is based on the analysis of 257 cases of proved bladder calculi and covers the period from 1939 to 1949.

There seems to be a prevailing opinion that the percentage of error in the roentgen diagnosis of bladder stone is relatively high. Lowsley and Kirwin [1] reported that shadows were not cast by the calculi in 35, or 61 per cent, of 59 cases. Hinman [2] stated that vesical calculi are frequently missed in the roentgenograms. Herman [3] believes that the failure of roentgen rays to disclose certain vesical stones in so many instances is due to invisibility of certain concretions, especially uric acid stones, the presence of overlying masses of hypertrophied prostatic tissue and the absence of gas from the rectum, which would serve to intensify the shadow of the stone. Wesson [4] stated that roentgen examination alone is not so dependable as cystoscopy, and Pelouze [5] mentioned that of the various methods of diagnosis, the outstanding one is the cystoscopic examination.

SEX

It is generally stated that bladder stones occur with much greater frequency in the male than in the female, and this has been confirmed by our experience. An analysis of this group of 257 cases shows that in 247 the patients were male and in 10 were female.

AGE

The youngest patient was 14 years old, and the oldest was 91. The incidence by decades is given in table 1.

From the Thomson Urological Fund and the Presbyterian Hospital of Chicago.

1. Lowsley, O. S., and Kirwin, T. J.: Clinical Urology, ed. 2, Baltimore, Williams & Wilkins Company, 1944, vol. 2.
2. Hinman, F.: The Principles and Practice of Urology, Philadelphia, W. B. Saunders Company, 1935.
3. Herman, L.: The Practice of Urology, Philadelphia, W. B. Saunders Company, 1938.
4. Wesson, M. B.: Urologic Roentgenology, ed. 2, Philadelphia, Lea & Febiger, 1946.
5. Pelouze, P. S.: Office Urology, Philadelphia, W. B. Saunders Company, 1940.

ANALYSIS OF CASES

A positive diagnosis of bladder stone was made from the plain film in 226, or 87.9 per cent, of the 257 cases. A critical review of these films revealed in six additional cases the presence of stones that were overlooked at the time of the first film reading. In eight cases rereading the intravenous urograms disclosed the presence of stones casting negative shadows.

ERROR IN FILM READING

In 31 patients the stones were not and could not be recognized on a review of the films, thus giving an error of 12 per cent.

We believe the following factors were responsible for our failure to recognize the presence of the stones: 1. In one case the stone had migrated into the urethra. 2. The stone was sometimes confused with the presence of a calcified fibroid. 3. A plain film was not made before the intravenous urogram was taken. 4. Sand was present in the bladder. 5. In one case the stone shadow was confused with a bowel shadow. 6. In eight cases of pure uric acid stones, five were not visualized, and three were seen as stones casting negative shadows on intravenous pyelograms.

TABLE 1.—*Age Incidence of Bladder Stones*

Age, Yr.	No. of Cases
14	1
21	1
31-40	11
41-50	15
51-60	31
61-70	74
71-80	51
81-90	72
91	1
	257

TABLE 2.—*Diagnosis of Bladder Stone*

	Number	Percentage
Total cases	257	100
Not diagnosed	31	12.1
Diagnosed	226	87.9
From plain films	212	82.5
From review of plain films	6	2.3
From negative shadow on intravenous pyelograms	8	3.1

We have recognized that bladder stones are easily visualized by cystoscopy, and no special effort has been made to visualize them with the use of roentgen rays. These observations are based on routine genitourinary films and intravenous pyelograms, and it is possible that with air cystography and a better preparation of patients the previously stated percentage of error could be lowered.

It has been stated many times that uric acid stones fail to cast shadows and hence are overlooked. This has not been our experience. Of the 18 cases in which stones failed to show shadows and in which chemical examinations of the stones were later made, in 13 the calculi were composed of either calcium phosphate or calcium oxalate or a combination of the two. In five cases the stones were pure uric acid. On the other hand, in three cases pure uric acid stones cast positive shadows in the roentgenograms.

SUMMARY

1. In our experience the incidence with which roentgenograms failed to show stones, while high (12 per cent), was not so high as mentioned by other authors.

2. In some cases the presence of stone shadows overlooked at first reading was demonstrated on a subsequent rereading of the film.

3. Pure uric acid stones were rare.

EVALUATION OF CYTOLOGICAL TECHNIC IN RECOGNITION OF MALIGNANT UTERINE NEOPLASMS

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and
R. T. Schmidt, M.D., Cleveland

After we had examined over 10,000 specimens from cervical and vaginal sites, we conducted an investigation to determine by objective study the existing accuracy of the cytological technic in this laboratory. Since the method is employed primarily as an aid in the recognition of cervical carcinoma, attention was directed toward the uterine cervix, and simultaneous cervical scraping and aspiration of the cervical canal were utilized in this series. The effectiveness of the technic in the recognition of cervical carcinoma in this institution will be evaluated.

BASES OF ANALYSIS

Those patients undergoing surgical procedures in the Department of Gynecology of the University Hospitals of Cleveland were selected for this study, and a specimen was obtained by the nursing personnel prior to each operative procedure. Aspirated material obtained from the cervical canal by means of a dry glass pipet was expressed onto the surface of a glass slide. A second glass slide was applied, and the two were compressed, thus spreading the material over the apposing surfaces of the two slides. These were then drawn apart, and the spreads were immediately immersed in the ether-alcohol fixing solution. In addition, scrapings obtained from the cervix by means of a tongue blade were spread over the surface of a third slide and immediately placed in the fixing solution.

Identified only by serial number, the slides were stained by the technic advocated by Papanicolaou,[1] with stain EA 36. The slides were examined objectively by one of us (J. W. R.) without knowledge of the clinical history or surgical findings. The criteria employed in the identification of malignant tumor cells are essentially those outlined by Papanicolaou and Traut.

To facilitate final statistical analysis and to allow a more critical evaluation of the technic, either of two interpretations was made. The first, designated (+), was limited to those specimens containing cells whose morphology was believed by the observer to warrant interpretation as malignant tumor cells. The second, designated (—), included those specimens which did not contain such cells or which, in the opinion of the microscopist, contained cells whose morphological features were insufficiently altered to justify the former classification.

From the Departments of Pathology and Gynecology of the University Hospitals of Cleveland.

This study was aided in part by a grant from the American Cancer Society, Ohio Division.

1. Papanicolaou, G. N., and Traut, H. F.: Diagnosis of Uterine Cancer by the Vaginal Smear, New York, Commonwealth Fund, 1943.

RESULTS

Taken throughout a period of nine months, 3,000 slides representing 1,000 consecutive specimens from 918 patients were examined. During the course of the study a total of 72 specimens were seen from patients with histopathological evidence of squamous cell carcinoma. Of these, an objective cytological interpretation of malignant tumor cells was possible in 71. The identification of adenocarcinoma was less satisfactory. While 34 specimens were submitted from patients proved to have adenocarcinoma, cytological recognition was possible in only 30. One patient with coexisting sarcoma and carcinoma was examined on two occasions, and in both instances anaplastic tumor cells were identified. Thus of 108 specimens from proved cases of malignant uterine neoplasm, cytological recognition was possible in 103. In six additional specimens, the cytological interpretation indicated the presence of carcinoma, while the histopathological findings were equivocal. Of the remaining 886 specimens, neither the cytological findings nor the material available for pathological examination disclosed evidence of malignant uterine neoplasms, although in many instances the surgical material available for correlation was inadequate as a basis for exclusion, and in 15 procedures no surgical specimens were submitted.

The findings in the presence of squamous cell carcinoma are shown in table 1. A total of 72 specimens from 55 cases of carcinoma were encountered. Regardless of whether correlation was made on the basis of cases or specimens, there was agreement of the cytological interpretation and the histopathological diagnosis, with one exception. This case, in which hysterectomy was performed for therapeutic termination of pregnancy, was studied by cytological means on one occasion, and the specimen submitted included only a scraping of the cervix, without aspiration of the cervical canal. Malignant tumor cells were not present

TABLE 1.—*Accuracy of Cytological Technic in Cervical Squamous Cell Carcinoma**

	Proved, Specimens	Cytology (+)	Proved, Cases	Cytology (+)
Well differentiated	5	5	5	5
Partially differentiated	31	31	21	21
Poorly differentiated	18	18	15	15
Undifferentiated	6	6	6	6
Carcinoma in situ	12	11	8	7
Unrecognized by cytological means	..	1	..	1
Total specimens	72	72	55	55

* Since many patients had several surgical procedures and thus more than one examination, correlation is shown for both the individual specimens and the cases.

in the specimen. Pathological examination of the surgical specimen disclosed a carcinoma in situ limited to the cervical canal and a uterine pregnancy of 3½ months. The failure of the cytological technic in this instance is attributed to the omission of the cervical aspiration.

The findings in the presence of adenocarcinoma are presented in table 2. Of 34 specimens with histopathological evidence of adenocarcinoma, cytological recognition was possible in only 30. These specimens were taken from 23 patients, of whom 21 were interpreted by cytological means to have malignant tumor cells. There are various causes for these errors. In two instances the presence of well differentiated adenocarcinoma was not apparent. One of these neoplasms was confined to the deeper layers of the endometrium

TABLE 2.—*Accuracy of Cytological Technic in Uterine Adenocarcinoma**

	Proved, Specimens	Cytology (+)	Proved, Cases	Cytology (+)
Well differentiated	7	5	4	3
Partially differentiated	22	21	15	15
Poorly differentiated	5	4	4	3
Unrecognized by cytological means	..	4	..	2
Total specimens	34	34	23	23

* Since many patients had several surgical procedures and thus more than one examination, correlation is shown for both the individual specimens and the cases.

and in all probability exfoliated few, if any, cells. Another well differentiated adenocarcinoma was not recognized because of the limited morphological alteration in the exfoliated cells. With the conditions imposed by this study, the specimen was considered as (—), although in actual practice it would be interpreted to contain atypical cells of endometrial origin. A specimen from one patient with a partially differentiated adenocarcinoma was correctly identified by cell studies at the time of endometrial curettage. Another specimen, taken at the time hysterectomy was done, was not so interpreted. The original histopathological sections taken from the uterus revealed no residual adenocarcinoma, although subsequent tissue did show the neoplasm. This failure obviously resulted from error in interpretation and illustrates the superior accuracy attained when multiple specimens are submitted and the analyses are based on cases rather than specimens. Another error was incurred in the presence of a poorly differentiated adenocarcinoma. The patient had a marked cervical stenosis which interfered with aspiration of the cervix. In this case, examination of vaginal fluid might have offered evidence of adenocarcinoma. Thus it is apparent that the causes for error in the cytological recognition of adenocarcinoma are more numerous and the results less accurate than in the recognition of squamous cell carcinoma.

The specimens submitted for pathological examination during the course of this study are recorded in table 3. Only in 268 cases could malignant uterine tumor be excluded by an examination of the uterus. When correlation with the uterine specimen was made, the cytological technic failed to demonstrate malignant tumor cells in two of 21 cases.

Although endometrial curettings were submitted in 444 instances, there was histopathological evidence of malignant uterine neoplasm in only 24. Of these, cytological recognition was possible in 21. The endometrial curetting failed to disclose the presence of adenocarcinoma in one instance, while the cytological specimen taken at the same time revealed malignant tumor cells. Results of subsequent curettage revealed an adenocarcinoma.

A total of 149 biopsy specimens were submitted during this study. Of these, 81 did not present evidence of carcinoma by either technic, while in 60 instances there was agreement between the histopathological and cytological technics in establishing the presence of squamous cell carcinoma. In two patients the cervical biopsy specimen did not contain squamous cell carcinoma on histopathological examination, while the cytological specimen taken at the same time indicated obvious carcinoma. Repeat biopsies in both cases proved the cytological interpretation to be correct. In addition, the cytological technic indicated the presence of squamous cell carcinoma in six instances, while the histopathological diagnoses were considered to be equivocal. The six instances represent three patients, from each of whom specimens for biopsy were taken on two occasions. Two of these patients were reported to have atypical hyperplasia of the cervical squamous epithelium on histopathological examination. The physicians concerned elected to treat these patients, and both are still being followed in this laboratory. The third patient was considered as having histopathological changes suggestive of squamous cell carcinoma. This patient was subjected to hysterectomy for other reasons, and careful examination disclosed no significant changes in the remaining squamous epithelium. Cell studies made at the time of hysterectomy did not show malignant tumor cells. Thus only these six specimens from three patients are considered as unproved or incorrect, since there is no conclusive evidence of carcinoma on histopathological examination.

TABLE 3.—*Correlation of Cytological Interpretation with Histopathological Diagnoses Made on the Submitted Surgical Specimens*

	Histopathological Examination	Cytological Interpretation	
Correlation with the uterine specimen			
Absence of malignant tumor by both technics	268	268	
Presence of malignant tumor by both technics	21	19	
Failure to detect malignant uterine tumors	0	2	
Totals	289	289	289
Correlation with endometrial curettings			
Absence of malignant tumor by both technics	444	444	
Presence of malignant tumor by both technics	24	21	
Cytology (+) without pathological evidence *	...	1	
Failure to detect presence of adenocarcinoma	1	3	
Totals	469	469	469
Correlation with cervical biopsy			
Absence of carcinoma by both technics	81	81	
Presence of carcinoma by both technics	60	60	
Cytology (+) without pathological evidence *	...	2	
Cytology (+) with equivocal pathological findings	6	6	
Failure to detect presence of carcinoma	2	0	
Totals	149	149	149
Correlation with miscellaneous specimens			
Absence of malignant tumor by both technics	78	78	78
No specimen submitted			
Cytology (—) without pathological examination	...	15	15
Grand total			1,000

* Repeat surgical biopsy in these cases revealed histopathological evidence of carcinoma.

A total of 78 specimens were submitted for pathological examination, which in no manner excluded the presence of carcinoma, and in 15 instances the surgical procedure was such that no specimen was submitted. Of these, cytological study failed to disclose malignant tumor cells.

An evaluation of the usefulness of the procedure in the recognition of cervical carcinoma was made independently by one of us (R. T. S.) in order to maintain some degree of objectivity. The clinical records on each case were reviewed, and the physician in charge was consulted in each instance.

Many of the patients had an obvious gross cervical lesion when first seen. These were immediately excluded since there was obvious indication for cervical biopsy. In some cases, a statement relative to the usefulness of the cytological technic in establishing the diagnosis was recorded in the hospital record. The physician concerned was contacted in each instance, and his opinion of the value of cytological interpretation was considered final. It should be noted that some physicians tended to be hesitant in giving credit to the method, and the final evaluation is a conservative estimate.

In a total of eight (14.5 per cent) of the cases of cervical carcinoma the condition was recognized initially by the cytological technic. In each instance an unequivocal cytological interpretation of carcinoma was made by the laboratory prior to the patient's hospitalization. Histopathological examinations revealed carcinoma in situ in four cases and an equal number of partially differentiated squamous cell carcinomas with evidence of invasion. Although the method was of value in the recognition of other cases, the suspicious nature of the cervical lesion was an indication for biopsy and the method served only as a confirmation of the clinical impression.

COMMENT

This controlled series of 1,000 consecutive specimens was examined for determination of the existing accuracy of the cytological technic in this laboratory. The variety of pathological lesions encountered during the nine months covered by this study served to impose a more critical evaluation of the method.

After considerable experience with the technic in the recognition of uterine carcinoma, it is apparent that the ultimate accuracy of the procedure depends only in part on the experience of the microscopist. Of equal importance is the nature of the specimen submitted, the care with which it is taken and the method of preparing the tissue spreads. The term "spreads" implies an even distribution of the secretion rather than a daub or smudge and, in our opinion, is preferable to the word "smear."

The importance of reduction of the number of so-called false positive interpretations is obvious, and, unfortunately, these are much more serious than the so-called false negative reports. The chances for error are reduced with a well prepared specimen which is representative of the site in question. The confirmatory biopsy similarly must be adequate if cervical carcinoma is to be excluded on the basis of histopathological examination. During the course of this study, two cases of cervical carcinoma were not apparent on initial biopsy. On the basis of the cytological findings, biopsy was repeated and a more adequate specimen was obtained. Histopathological examination of the second specimen revealed obvious squamous cell carcinoma in each instance.

Only six specimens from three patients were interpreted to contain malignant tumor cells by cytological identification without confirmation by surgical biopsy. There was definite cytological evidence of squamous cell carcinoma in each of these specimens. These instances must be considered unproved or incorrect interpretations on the basis of the equivocal pathological findings. Two of the three cases are still being followed in this laboratory, and at this time there is no definite cytological evidence of malignant tumor cells.

SUMMARY AND CONCLUSIONS

1. In a controlled series with material obtained directly from the uterine cervix and cervical canal, there was objective cytological recognition in 103 of 108 specimens, with proved malignant uterine neoplasm.

2. By experience with the method, the frequency of the so-called false positive cytological interpretations can be reduced; only six specimens were so interpreted in this series without histopathological confirmation.

3. The cytological technic is useful in the identification of uterine neoplasms and may reveal the presence of lesions unrecognized with the use of endometrial curettage or cervical biopsy.

4. A total of eight (14.5 per cent) of the cases of cervical squamous cell carcinoma observed during the course of this study were recognized initially by the cytological technic.

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CLINICAL NOTES

PHYSIOLOGICAL REACTION TO PITUITARY ADRENOCORTICOTROPIC HORMONE (ACTH) IN SEVERE BURNS

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I have been led to believe, through Selye's works,[1] that "sudden stimuli to which the organism is not quantitatively or qualitatively adapted bring on the alarm reaction and the general adaptation syndrome." Probably the best method of eliciting a response of such great magnitude is the production of severe burns, irrespective of the mechanism of initiation. Extensive burns are usually associated with certain physiological phenomena:

1. Severe pain
2. Fever
3. Shock and toxicity
4. Increased cellular permeability (oozing) and decreased renal function
   - (*a*) Loss of sodium and chloride
   - (*b*) Loss of fluids
   - (*c*) Loss of protein
   - (*d*) Retention or loss of potassium, depending on the degree of the protein catabolic state and the magnitude of the sodium loss
5. Hemoconcentration
6. Suppuration and infection
7. Loss of appetite, hypoproteinemia and negative nitrogen balance
8. Progressive anemia
9. Excessive granulation tissue and excessive fibroblastic proliferation
10. Inhibition of epithelization.

There is substantial evidence covering a wide area of medicine which indicates that all these phenomena may be inhibited or reversed by adequate physiological adrenal cortical stimulation with pituitary adrenocorticotropic hormone (ACTH).[2] The fact that they are not inhibited or reversed has led me to believe that the alarm reaction and general adaptation syndrome in the case of massive burns are not capable of coping adequately with an overwhelming thermal insult. This may be considered primarily as a failure of endogenous adrenocorticotropic hormone to meet this long period of crisis. To test the above premise it was decided to treat a patient with severe burns (over 60 per cent of the body surface involved) with substantially nothing other than the hormone, for according to a recent statistical evaluation of 794 patients in all age groups who had thermal burns it was found that there was little or no chance of their survival under conventional management when over 60 per cent of their body surface was involved.[3]

On practical as well as theoretical grounds I thought it best to study the total metabolic and physiological changes taking place within the body from the time of the initial insult through the complete recovery phase, rather than to limit an investigation to any specific period or to any isolated type of reaction.

REPORT OF A CASE

First 24-Hour Period After Injury, Including Hospitalization.—T. G., a normal, healthy 23 year old Spanish-American man received severe gasoline burns on May 19, 1950 at 12:45 p. m.[4] He was taken to a local hospital within an hour, where it was estimated that 90 per cent of the body was burned. Routine care was immediately instituted. The burned areas were cleaned and pressure dressings applied. During the first 24 hours plasma was continuously given by the

From St. Monica's Hospital.

Dr. John R. Mote of Armour Laboratories assisted me and provided the pituitary adrenocorticotropic hormone used in this study.

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4. Whitelaw, M. J., and Woodman, T. W.: The Treatment of Severe Burns with ACTH, J. Clin. Endocrinol. **10**: 1171, 1950.

intravenous route, a total of 9,000 cc., together with 2,000 cc. of 5 per cent dextrose in isotonic sodium chloride solution. An additional 5,000 cc. of fluid was given orally. A Foley indwelling catheter was inserted on admission, and 900 cc. of urine was recovered in the first 24 hours. It was estimated that during the first 24 hours after the injury the patient lost approximately 10,000 cc. of fluid through surface weeping. He received 1,800,000 units of penicillin, 500 mg. of meperidine (demerol®) hydrochloride and ½ grain (0.03 Gm.) of morphine sulfate during this period. At the end of 24 hours he was flown to Phoenix, Ariz., 200 miles away, where he was hospitalized (early in the afternoon of May 20, 1950).

Second Hospitalization.—At Phoenix the patient was hospitalized in an open seven bed ward and received only general ward care. He appeared to be in mild shock. The temperature was 102 F., and the pulse rate was 105 per minute and slightly thready. Blood pressure readings were not obtainable because of the compression bandages. On admission an evaluation of the adrenal cortical response to the burn stimulus was made with a direct phloxine eosinophil count. This showed complete disappearance of circulating eosinophils. Administration of pituitary adrenocorticotropic hormone, 20 mg. every six hours intramuscularly, was begun immediately and no other medicament was employed other than 1 Gm. of ascorbic acid (vitamin C) intramuscularly twice daily and morphine sulfate, ¼ grain (0.015 Gm.) as necessary. Fluid intake and output were recorded, and total urine chloride, creatinine, urea nitrogen, protein and 17-ketosteroids were determined. Serial blood and serum determinations were done (tables 1 and 2; figs. 1-3).

TABLE 1.—*White Blood Cell Count and Differential**

Day	WBC	Juvenile	Stab.	Seg.	Lymph.	Mono.	Eosin.
1	26,500	..	21	69	6	4	..
2	10,700	..	12	74	12	1	1
3	10,450	..	14	63	17	4	2
4	9,900	..	8	73	14	5	..
5	9,200	..	4	71	20	5	..
6	8,700	..	12	70	13	5	..
7	16,450	..	19	75	5	..	1
8	19,250	..	5	81	13	..	1
9	17,400	..	13	74	9	4	..
10	23,050	..	8	72	11	7	2
11	24,000	..	15	68	31	1	..
12	27,900	..	13	67	20	..	..
13	25,200	..	2	76	22	..	..
14	17,850	..	7	73	13	7	..
15	14,400	..	6	64	26	2	2
16	21,000	4	6	66	16	8	..
17	18,800	1	5	76	7	11	..
18	21,500	1	6	68	14	11	..
22	23,200	..	26	54	11	9	..
25	9,350	..	..	64	28	8	..
28	9,600	..	..	70	26	4	..
32	10,700	..	2	72	24	2	..

* Note the marked effect of hemodilution.

First to Fifth Hospital Day: Pain was strikingly diminished, and only 3¾ grains (0.245 Gm.) of morphine sulfate were required over the first five day period. Fever was rapidly diminished, and only mild hyperpyrexia persisted during this time. Shock did not appear. Toxicity was minimal; in fact, the patient had a sense of extreme well-being. Oozing decreased progressively, so that there was essentially no evidence of active oozing when the bandages were removed on the fifth day.

Kidney function was increased early, as evidenced by increase in volume and disappearance of microscopic abnormalities. Chloride excretion remained extremely low during the entire period. Hemoconcentration was not present at any time. Hemodilution was evident in the hematocrit and total proteins. Suppuration and infection were minimal, and tissues were clean and dry after removal of bandages on the fifth day. The patient had an excellent appetite and took all fluids and food by mouth during this time. By the fifth day he was consuming food equal to 3,000 calories daily, over 100 Gm. of which was protein. His weight remained essentially stable. Mild hypoproteinemia was recorded. The nitrogen balance was interpreted as approaching equilibrium during the period. Anemia was present but was attributed in part to hemodilution.

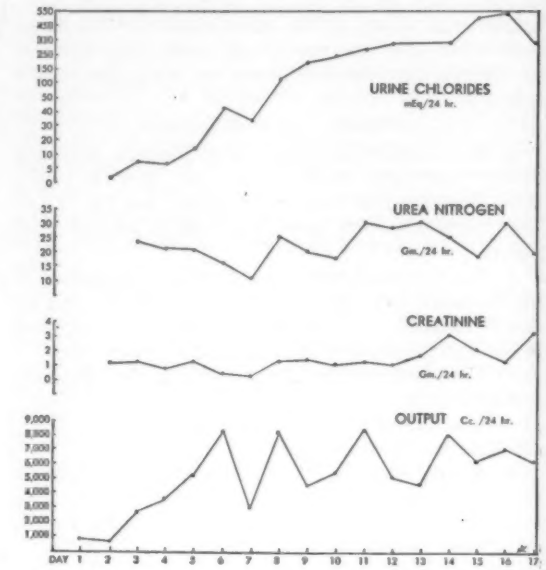

Fig. 1.—Total 24 hour urinary chlorides, urea nitrogen, creatinine and urinary flow.

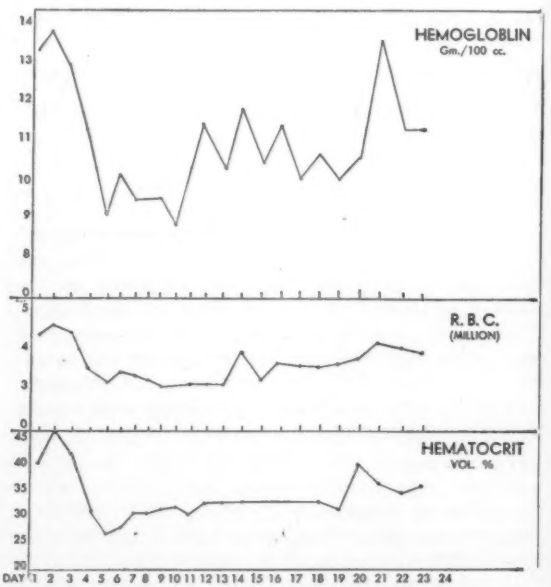

Fig. 2.—Graph showing the abrupt fall in hemoglobin, red blood cells and hematocrit during the first five days after initial insult.

On removal of dressings on the fifth day, with the patient in the upright position (he had received no narcotics), fibroblastic proliferation was not noted and epithelization was evident over all areas except the torso and right thigh and leg. At this time a careful estimate was made of the extent

of the burned surface area, which was done by use of paper patterns to matching the burns. These measured 1.16 square meters. The man weighed 160 pounds (72.6 Kg.), and his height was 69 inches (175 cm.). The total surface area by Boothby and Sandiford standards is 1.64 square meters. He therefore suffered burns of 70.7 per cent of his total surface area. Examination now revealed first degree burns of the neck and face as well as of the lips and nose. Second degree burns involved the anterior surface of the right thigh, over half of the left leg, and the genitalia. Both upper extremities were over 50 per cent involved, except for the right antecubital region and a small adjacent area on the right forearm. Third degree burns were present over the entire trunk above the belt line, the entire posterior surface of the right leg, the lower portion of both buttocks and the thumbs and thenar eminences of both hands. Petrolatum gauze pressure dressings were then reapplied.

Sixth to Seventeenth Hospital Day: The dose of pituitary adrenocorticotropic hormone was maintained at 20 mg. every six hours intramuscularly. The temperature rose on the seventh day, and an intercurrent pneumonitis of the right lung was detected. Over the eighth to ninth days the patient received 3 units of plasma and 2.25 Gm. of aureomycin hydrochloride. The hormone dose was raised on the tenth day to 25 mg. every six hours intramuscularly, and no further antibiotics or intravenous therapy was employed. The pneumonitis cleared uneventfully within one week. Pain during this period was relatively nonexistent, as the patient required only 2½ grains (0.15 Gm.) of morphine sulfate. Hyperpyrexia was minimal except for days 8 to 11, when the pneumonitis was active. Shock and toxicity were absent.

The patient no longer looked or acted sick. There was little oozing and suppuration was essentially nil. Urinary output approximated fluid intake, and chloride excretion steadily increased. The patient's appetite was ravenous; he consumed food equal to 5,000 or 6,000 calories a day after the fifteenth day. On the twelfth hospital day, because of the time required to feed him, a private duty nurse was assigned for eight hours daily, although he remained on the ward. Total protein reached its lowest point on the seventh hospital day, when there was a decided reversal in the albumin-globulin ratio. During this phase of hypoproteinemia there was no clinical evidence of edema nor any effect on kidney function. Protein supplied in the form of 3 units of plasma did not significantly alter the urea nitrogen output or the total blood protein.

On the seventeenth day the dressings were removed. The surfaces were noted to be clean and dry. The patient was able to stand and take a few steps. Epithelization of the torso or right leg had not begun.

Eighteenth to Forty-First Hospital Day: Improvement during this period was rapid. No further narcotics or analgesics were required, and the patient was essentially free from pain. The temperature remained normal after the twenty-fifth day. The patient was ambulatory during this period after the thirtieth day, in spite of the exposed muscle surface of the right leg. Pituitary adrenocorticotropic hormone was gradually tapered off to 10 mg. every six hours intramuscularly by the thirty-second day and was maintained at this dosage until the ninety-second day of observation. Epithelization had not begun on the torso or the leg during this period, but all other areas had become epithelized. Fibroblastic proliferation remained minimal.

Forty-Second to One Hundred Tenth Hospital Day: Pain, fever and toxicity were absent during the remainder of the period of observation except for a short time after surgical intervention for an acute abdominal condition on the forty-seventh day. Wound healing appeared to be essentially normal after the operation.

On the forty-second hospital day epithelization began on the torso and spread rapidly. Coalescence of large areas was noticed within one week. By the ninety-second day epithelization of the torso was complete. The skin of the back was of normal texture. Melanin deposits were extremely intense, particularly at the belt line, with various degrees of hyperpigmentation throughout the new skin. The second degree burn areas were now deeply pigmented and, although soft, were in some areas elevated approximately 3 mm. above the surface. Biopsies of these were taken for study.

Inasmuch as it was now evident that the depth of the burns involving the right thigh and leg precluded the possibility of any regeneration of epithelium from the deeper layers, we

TABLE 2.—*Fluid Intake and Output and Urine Determinations in Reported Case*

Hospital Day	Total Volume (Cc.)		Total Chlorides mEq./ 24 Hr.	Total Creatinine Gm./ 24 Hr.	Total Urea Nitrogen Gm./ 24 Hr.	17-Ketosteroids Gm./ 24 Hr.	Total Protein Gm./ 24 Hr.	Microscopic/HPF			
	Intake	Output						WBC	RBC	Casts	Specific Gravity
1	16,000	900	...	....	....	....	....	...	...	.....	.....
2	.....	815	1.4	1.01	....	....	....	2-3	6-7	Occ.*	1.023
3	5,080	2,780	7.7	1.20	24.9	....	1.12	...	...	.....	.....
4	5,565	3,715	6.1	0.95	21.9	....	0.84	...	...	.....	.....
5	6,270	5,370	13.2	1.22	21.4	....	1.16	Occ.†	0	0	1.008
6	6,160	8,450	41.8	0.68	16.9	....	1.35	...	...	.....	.....
7	7,955	3,000	34.7	0.48	11.4	24.2	0.60	...	...	.....	.....
8	8,905	8,410	109.3	1.26	25.7	....	1.68	Occ.†	0	0	1.004
9	8,335	4,875	196.2	1.54	20.5	....	....	...	...	.....	.....
10	7,730	5,660	238.2	1.11	18.9	....	....	...	...	.....	.....
11	6,505	8,650	260.7	1.38	31.1	....	1.47	...	...	.....	.....
12	8,075	5,250	302.9	1.05	29.7	....	0.79	Occ.†	0	0	.....
13	6,080	4,950	...	1.88	31.7	....	....	...	...	.....	.....
14	6,500	8,150	305.6	3.26	27.7	....	....	...	...	.....	.....
15	7,100	6,350	496.6	2.10	19.4	32.6	....	...	...	.....	.....
16	6,280	7,050	528.7	1.41	31.4	....	....	...	...	.....	.....
17	6,610	6,300	333.9	1.32	21.1	....	....	2-3	0	0	1.008
18	5,645	6,300	...	....	....	....	....	...	...	.....	.....
19	5,410	5,100	...	....	....	....	....	...	...	.....	.....
20	5,200	4,500	...	....	....	....	....	...	...	.....	.....
21	4,790	4,200	...	....	....	....	....	...	...	.....	.....
22	5,500	5,300	...	....	....	....	....	...	...	.....	.....
23	4,390	6,000	...	....	....	....	....	...	...	.....	.....
24	5,860	5,150	...	....	....	....	....	...	...	.....	.....
25	6,165	5,200	...	....	....	....	....	...	...	.....	.....
26	5,840	4,500	...	....	....	....	....	...	...	.....	.....

* Occasional fine granules. † Occasional white blood cells.

decided to proceed with the second part of the experiment. An attempt was made to evaluate the effect of pituitary adrenocorticotropic hormone in blocking the antigen-antibody response by the use of homografts.

Forty homologous pinch grafts from two donors were applied (by Dr. Thomas W. Woodman) to the right thigh and leg on the forty-third day. When dressings were removed eight days later, 39 of the 40 grafts were observed to have taken. Furthermore, concentric spread of epithelium from the graft sites was noted at this time. Rapid epithelization of the thigh and leg occurred during the next fourteen days. Epithelization of the thigh and leg was complete by the one hundred first day. Pituitary adrenocorticotropic therapy was discontinued on the ninety-second day, after which some fibroblastic proliferation occurred. In spite of this no limitation of motion or contractures developed. Several skin biopsies were done during this period and will be reported later.

One Hundred Tenth to One Hundred Seventieth Days After Injury: During this time the patient was rehospitalized for three weeks of pituitary adrenocorticotropic therapy for

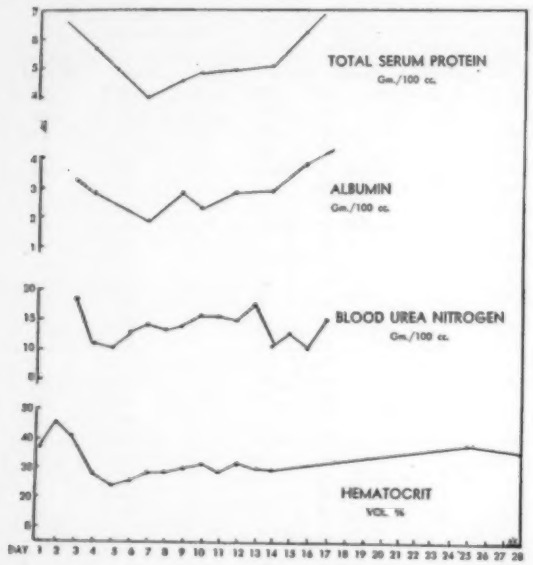

Fig. 3.—Graph illustrating the effects of hemodilution on serum protein, albumin, blood urea nitrogen and hematocrit.

study of the effect of this therapy on the mild fibroblastic proliferation. He was given 80 mg. daily for 21 days, at the end of which time it was observed that these areas were definitely flatter and smoother.

COMMENT

This case illustrates my concept that circulating endogenous adrenocorticotropic hormone is quantitatively insufficient to meet the acute stress of severe burns. When the normal adrenal cortex is adequately stimulated by administration of exogenous adrenocorticotropic hormone the physiological phenomena usually present in severe burns are either eliminated or appreciably reduced. Four other patients have responded in like manner; data will be reported later.[5] My results have since been substantiated by others.[6]

The concept that pituitary adrenocorticotropic hormone would block the antigen-antibody response of the skin and so make homograft transplants possible was tested by applying 40 homologous pinch grafts from two donors to the completely denuded areas of the right leg on the forty-third day. Within 58 days the grafts not only had taken but had grown to epithelize the entire area.

Management of this case with pituitary adrenocorticotropic therapy further illustrates the tremendous saving in both medical personnel and supplies as compared with the conventional methods[7] (fig. 4). In the light of the present world situation I believe that my results with pituitary adrenocorticotropic hormone (ACTH) in the management of this and other severely burned patients call for an immediate reevaluation of

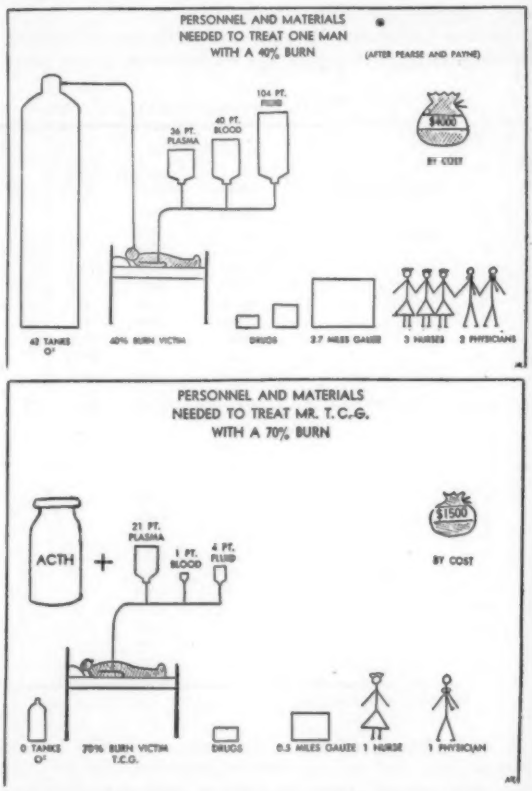

Fig. 4.—Charts comparing cost of conventional treatment of 40 per cent burn with cost of pituitary adrenocorticotropic hormone treatment of 70 per cent burn.

methods of treatment of such patients. At the fundamental level, my results not only provide a tool for understanding of the action of pituitary adrenocorticotropic hormone but could conceivably open up an entirely new vista in transplantation and plastic surgery.

5. Whitelaw, M. J.: The Treatment of Severe Burns with ACTH: Preliminary Case Reports, in Mote, J. R.: Proceedings of the Second Clinical ACTH Conference, Philadelphia, The Blakiston Company, to be published.

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COUNCIL ON PHYSICAL MEDICINE AND REHABILITATION

REPORT OF THE COUNCIL

The Council on Physical Medicine and Rehabilitation has authorized publication of the following report.

The Council wishes to express its appreciation for the valuable cooperation of the Advisory Committee on Electrocardiographs for its expert services. The Committee members are: Drs. Howard Burchell, George Fahr, Harold Feil, Harold E. B. Pardee, William D. Stroud and Carl J. Wiggers.

HOWARD A. CARTER, *Secretary.*

SUGGESTIONS FOR PROSPECTIVE PURCHASERS OF ELECTROCARDIOGRAPHS

Acceptance of an instrument by the Council on Physical Medicine and Rehabilitation carries with it assurance that fundamentally the design and construction of the instrument is such that it will produce adequate records for clinical diagnoses, assuming that no defects have developed and it is properly used. However, the Advisory Committee on Electrocardiographs stress that the possession of knowledge concerning basic electrophysical principles and skill in the technic of operating an electrocardiograph is as essential for the procurement of accurate records as is the type of instrument itself.

Since special types of electrocardiographs have advantages in certain places and situations, the following points may be mentioned as a partial guide to a physician about to purchase an electrocardiograph:

1. *General.*—The prospective purchaser should make a general assay as to his specific need for an electrocardiograph and whether the majority of the patients on whom tracings will be taken will be in his office or at a home. He should know whether he is likely to encounter situations where no alternating house current is available. He should give some attention to the weight and portability of the instrument and the apparent sturdiness of its construction.

2. *Availability of Service.*—With all electrocardiographs, but particularly with amplifying units, the prospective purchaser should satisfy himself as to the service facilities in, or to, the region he practices.

3. *Ease of Operability.*—The ease of operability is related to what may be called functional design of the panel. Are the power and camera switches sufficiently different or separated so that they will not be mistaken for each other? Are the standardization switch and sensitivity control conveniently located to one another as an operating unit? Are the camera switch and centering control, if one is present, conveniently located so as to be used at about the same time? Are the centering control and sensitivity control so placed as not to be easily confused? What delay occurs between the recording of the different leads? How easily is the recording paper reloaded? Does the paper run at correct speed as checked by the timer? These questions more specifically pertain to amplifying instruments but in principle may be applied, in part at least, to any type of electrocardiograph.

4. *Protection Against Misuse.*—While there is little excuse for one's operating an instrument contrary to directions, it may be assumed to occur. For instance, in direct writers, is there protection to writer arm if the lead selector switch should be turned to an unconnected lead wire, or will it vibrate dangerously so as to cause breakage? If the instrument is connected with a wrong polarity to a wall outlet, is there any possibility of discomfort to the patient? How sensitive is the instrument to lamps or appliances utilizing alternating current? It may be worth while to test the instrument in the office where it is to be used.

5. *Special Instances.*—It is desirable that any physician wishing to use an electrocardiograph under special conditions, such as in an operating room or in a laboratory where other apparatus may also be attached to the patient, make a search into all possibilities of casualty hazards with specialized consultants if necessary.

The Council on Physical Medicine and Rehabilitation has authorized publication of the following article.

HOWARD A. CARTER, *Secretary.*

AN APPRECIATION

The Council on Physical Medicine and Rehabilitation expresses its appreciation of the services of the following consultants, who so freely gave their assistance in the work of the Council during the year 1950: Drs. Conrad Berens, Edward Bigg, Raymond Carhart, Mrs. Eva Thompson Carson, Drs. Richard K. Cook, G. de Takats, Donald J. Erickson, David C. Fainer, Alan R. Feinberg, Theodore Friedemann, Clarence J. Gamble, A. S. Gordon, John S. Hibben, John Huffman, I. F. Hummon, Ernest E. Irons, Mary Karp, Louis R. Krasno, Margarete M. Kunde, Alfred Lewy, Clayton Loosli, A. M. Mackay, Gordon Martin, C. O. Molander, Keron C. Morrical, L. A. Nalefski, Louis B. Newman, A. M. Olsen, Benjamin H. Orndoff, Stafford L. Osborne, Howard F. Polley, H. G. Poncher, Charles E. Pope, Mr. Luther Ramer, Drs. John Reichert, Joseph Remlinger, Wilbur Rucker, Robert S. Schwab, Steven O. Schwartz, S. Richard Silverman, Ralph Taraba, O. E. Van Alyea and H. O. Wernicke.

American Health Resorts.—Drs. F. A. Hellebrandt, M. B. Jarman, Walter S. McClellan and Euclid M. Smith.

Artificial Limbs.—Drs. Rufus H. Alldredge, Henry H. Kessler, Paul E. Klopsteg, Messrs. J. B. Korrady and Lucius Trautman.

Audiometers and Hearing Aids.—Drs. Gordon Berry, Hallowell Davis, Kenneth M. Day, Edmund P. Fowler, Isaac H. Jones, Dean Lierle, Moses H. Lurie, Douglas Macfarlan, C. Stewart Nash and Paul E. Sabine.

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Education.—Drs. Frances Baker, Robert L. Bennett Jr., Ben L. Boynton, Earl C. Elkins, Robert W. Johnson Jr., H. Worley Kendell, M. E. Knapp, Richard Kovacs, Sedgwick Mead, Fred B. Moor, William H. Northway, Winfred Overholser, Donald L. Rose, William H. Schmidt, Walter M. Solomon, William D. Stroud, Arthur L. Watkins, George D. Wilson and Charles S. Wise.

Electrocardiographs.—Drs. Howard B. Burchell, George Fahr, Harold Feil, Harold E. B. Pardee, William D. Stroud and Carl J. Wiggers.

Electroencephalography.—Drs. P. Bailey, Edward J. Baldes, Hallowell Davis, Frederic A. Gibbs, Franc Douglas Ingraham and Herbert H. Jasper.

Ophthalmic Devices.—Drs. Thomas D. Allen, David G. Cogan, William F. Hughes Jr., Richard G. Scobee and Kenneth C. Swan.

Respirators.—Drs. Edward L. Compere, William T. Green, Warren E. Wheeler, James L. Wilson and James L. Whittenberger.

Roentgen Rays and Radium and the Medical Aspects of Atomic Energy.—Drs. W. Edward Chamberlain, Arthur C. Christie, Kenneth S. Cole, L. F. Curtiss, Edwin C. Ernst, Hymer L. Friedell, Robert R. Newell, Eugene P. Pendergrass, U. V. Portmann, Edith H. Quimby, Lauriston S. Taylor, Stafford L. Warren and J. L. Weatherwax.

THE JOURNAL
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REGISTRATION OF PHYSICIANS JANUARY 15

A special registration of physicians, dentists and veterinarians will be held on Jan. 15, 1951. On that date all such persons who have not reached their fiftieth birthday except members of the regular or reserve components of the uniformed services and certain categories of aliens will be registered unless they are already registered under the Oct. 16, 1950 registration. In this issue of THE JOURNAL there are several references to the registration of physicians and the status of reserve officers. In the Washington News and the Government Services section may be found information provided either by the Washington Office of the American Medical Association or by a press release from the Department of Defense. All of this information is important to the medical profession, especially men under 50 years of age who must register Jan. 15, 1951. Also, it is important to reserve officers.

Of particular interest are the procedures for calling medical men into service: The Army, Navy and Air Force will periodically submit to the Secretary of Defense their proposals for ordering reservists into active military service. These proposals will be considered by the Director of Medical Services, Dr. Richard L. Meiling, who will obtain the comments of the Armed Forces Medical Advisory Committee of the Department of Defense and the National Resources Advisory Committee of the National Security Resources Board. The final decision on the proposals will be made by the Secretary of Defense. The National Advisory Committee will advise the Selective Service System and help coordinate the work of state and local volunteer advisory committees with respect to the selection of physicians, dentists and allied specialists.

THE JOURNAL and the Council on National Emergency Medical Service of the American Medical Association will keep readers advised of developments in this field as they occur.

STUDENT AMERICAN MEDICAL ASSOCIATION

The House of Delegates of the American Medical Association has urged the creation of a Student American Medical Association. Student delegates from 48 medical schools throughout the United States met in Chicago on December 28 and 29 to organize such an association. Its objectives are to advance medicine, contribute to the welfare and education of medical students, familiarize its members with the purposes and ideals of the medical profession and prepare its members to meet the social, moral and ethical obligations of the profession.

Before the meeting adjourned, 13 schools had ratified a constitution. Delegates representing the other schools deferred ratification for no more than 60 days, so that opportunity might be given to study of the constitution at the schools from which they came.

Warren R. Mullen of Jackson, Mich., a student at the University of Michigan Medical School, Ann Arbor, was elected president; Harry W. Sandberg of Moline, Ill., a student at the University of Illinois College of Medicine, Chicago, vice president, and David Buchanan of Huron, S. D., a student at the University of South Dakota School of Medical Sciences, Vermillion, treasurer. Leo E. Brown of Harrisburg, Pa., is the executive secretary and will make his headquarters at the American Medical Association in Chicago.

Elected as members of the executive council were Bill Davenport, Clinton, Ark. (University of Arkansas School of Medicine, Little Rock); Herbert Sperling, Great Neck, Long Island, N. Y. (Boston University School of Medicine); John W. Looper, Augusta, Ga. (Medical College of Georgia, Augusta); Donald J. Brugger, Alliance, Ohio (Ohio State University College of Medicine, Columbus); J. Allan Henderson, Hood River, Ore. (University of Oregon Medical School, Portland); Charles Wilson, Galveston, Texas (University of Texas School of Medicine, Galveston); Howard J. Christian, Newton, Mass. (Tufts College Medical School, Boston).

In the Organization Section of this issue of THE JOURNAL is a picture of the officers of the association.

The association will consist of academic societies in medical schools of the United States approved by the Council on Medical Education and Hospitals of the American Medical Association. Each school can have one society, which must have a membership of at least one fourth of the students or 85 students, whichever is the smaller. Each society will have equal rights and representation in the Student American Medical Association House of Delegates, which will determine the policies of the association. Academic societies will determine the qualifications of their own membership, but the constitution and by-laws prohibit refusal of membership on the basis of race, religion, color or sex.

Interns may be admitted to membership at the discretion of the local student society.

Executive authority will rest in an executive council composed of the elected officers (president, vice president and treasurer), seven student councilors and three senior councilors. The 10 students will be the elected representatives of the students, whereas the three senior councilors will be named by the American Medical Association. The latter organization will provide an executive secretary and headquarters office in Chicago.

An advisory committee to each constituent society will be composed of the dean of the medical school or his appointed representative, two faculty members elected by the students, a county medical society representative and a state medical society representative.

The executive council of the student association, with the approval of its House of Delegates, may raise funds by levying annual dues on each academic society on the basis of the membership as of April 1, the amount to be specified by the by-laws of the House of Delegates. This was fixed initially at $1 per student membership.

Until the student association deems it advisable to issue its own publication, space will be made available for this organization in THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION.

The Student House of Delegates will name two members as its representatives to the American Medical Association House of Delegates. A proposal to change the constitution of the American Medical Association to provide such representation will be considered at the annual meeting in Atlantic City in June 1951.

When the House of Delegates formally called for the creation of a student association, action was initiated immediately to provide for a meeting of student delegates from the medical schools. The December 1950 meeting reflected the promptness with which the wishes of the House were met and indicated the keen desire on the part of many medical students to participate in medical affairs of common interest. The Chicago session was well attended and the program was seriously and ably presented from beginning to end. The students who participated deserve credit for the forcefulness and foresight in their deliberations. They can be assured, as they were during their meeting, of the warm welcome awaiting them from the members of the American Medical Association. As time progresses and the Student American Medical Association grows, there will be increasing opportunities for students and practitioners to view together their problems of common interest and for one group to observe the problems of the other. As is true for the American Medical Association, the success of the students' organization must come from local areas where the programs are initiated and the foundation laid for carrying them to completion.

DEFEAT FOR THE ANTIVIVISECTIONISTS

In the recent November elections, the citizens of Los Angeles voted 357,393 to 261,699 to permit unclaimed cats and dogs in the city to be used for experimental purposes. The referendum, known as Proposition C, arose from a demand by the antivivisectionists in the spring of 1949 that the city council issue an ordinance prohibiting the use of pound dogs in research. A public hearing on the matter was held on April 19, at which testimony from the antivivisectionists and from eminent scientists of the Los Angeles area was heard. While the plea of the antivivisectionists was thrown out, this hearing drew attention to the necessity for positive action to insure the availability of an adequate supply of animals for experimental purposes. Consequently, the city council, to the chagrin of the antivivisectionists, passed an ordinance on July 21 permitting the use for research purposes of animals from the city pound. Whipped into activity by the manner in which their efforts had rebounded, the antivivisectionists entered two suits to enjoin the city from putting the new ordinance into effect and were successful in obtaining a temporary injunction. They then obtained sufficient signatures to invalidate the ordinance and to call for a referendum. The city council, at the suggestion of the Medical Research Association of California, decided to repeal the ordinance and place the issue in the hands of the voters in the November 7 election. Vigorous campaigns were carried on by both the antivivisectionists and the supporters of medical research. It is worth noting that the antivivisectionists probably cut the margin of votes considerably by a last minute coup, in which they adopted the billboard picture which the medical science supporters had displayed, having merely altered the wording from "Vote Yes on C" to "Vote No on C"; thus many of the voters became confused, thinking a "no" vote would protect the interests of medical science.

The antivivisectionist cause suffered two other setbacks in the November elections. In Baltimore the proposed charter amendment to prohibit the experimental use of city pound dogs was defeated by a score of 160,000 to 38,000, while in Illinois, where a bill to permit use of pound animals for research was defeated by the 1949 session of the legislature, a number of the opponents of that bill went down in defeat. These three encouraging election results promise to have considerable effect on the legislation in prospect in the near future in New York, Pennsylvania, Ohio, Illinois, Wisconsin, South Dakota, Colorado and Arizona. This is no time, however, for complacency on the part of supporters of medical research. Events of the past year have proved that, if the public is properly informed of the necessity of animal experimentation, the antivivisectionist threats to medical progress can be nullified. The National Society of Medical Research, which is supported by 133 member organi-

zations, is actively engaged in combating the attempts of the antivivisectionists to throttle medical research and in promoting legislation designed to insure the supply of experimental animals. Other similarly motivated groups have been organized locally to help solve local problems. Such organizations can be very effective under proper leadership and deserve the consideration and support of all members of the medical profession.

ACTH AND CORTISONE

The now often quoted opinion that pituitary adrenocorticotropic hormone (ACTH) and cortisone do not cure anything are probably correct according to Hench.[1] Investigators so far have failed to explain how these substances work. Hench stresses that both agents affect not the cause of a disease but the reaction of the tissue to the irritant or the cause. The dominant influence, as he sees it, is on the pathologicophysiological changes or the disease itself rather than on the pathologicoanatomic changes or on the causative factor of these conditions.

In a recent symposium Hench emphasized that what is striking about these two hormonal substances is that they are the first natural agents by means of which it has been possible to demonstrate the potential reversibility of several diseases, especially rheumatoid arthritis. This remarkable, although temporary, effect was observed in rheumatic fever, acute rheumatic carditis, disseminated lupus erythematosus and certain allergic conditions.

Slocumb and his associates[2] of the Mayo Clinic report in this symposium on 23 patients with severe or moderately severe rheumatoid arthritis treated with these hormonal substances. The antirheumatic effect was dramatic in 13, less dramatic in nine and moderate in one. When the use of either hormone was discontinued a relapse generally occurred, sometimes promptly, sometimes slowly. Eight patients maintained 60 to 90 per cent of the improvement for seven to 14 months. Five patients maintained about 50 per cent of the improvement. The other 10 patients maintained little or none of the improvement. Barnes[3] treated seven patients with acute rheumatic fever with cortisone and three patients in their first attack of rheumatic fever with pituitary adrenocorticotropic hormone. The treatment did not prevent recurrences of the disease and did not modify the preexisting chronic valvular damage and associated cardiac hypertrophy. Three patients with hay fever and bronchial asthma sensitive to ragweed pollen showed prompt relief from the symptoms. The relief of symptoms, however, was confined to the period during and immediately following the time when cortisone was being administered.

1. Hench, P. S.: Introduction: Cortisone and ACTH in Clinical Medicine, Proc. Staff Meet., Mayo Clin. **25**: 474 (Aug. 16) 1950.
2. Slocumb, C. H.; Polley, H. F.; Hench, P. S., and Kendall, E. C.: Effects of Cortisone and ACTH on Patients with Rheumatoid Arthritis, Proc. Staff Meet., Mayo Clin. **25**: 476 (Aug. 16) 1950.
3. Barnes, A. R.: Effects of Cortisone and ACTH in 14 Patients with Acute Rheumatic Fever, Proc. Staff Meet., Mayo Clin. **25**: 478 (Aug. 16) 1950.
4. Sprague, R. G.: Summary: Cortisone and ACTH in Clinical Medicine, Proc. Staff Meet., Mayo Clin. **25**: 500 (Aug. 16) 1950.

The importance of the observations of Hench, Kendall, Slocumb and Polley, according to Sprague,[4] rests chiefly on the initial physiological observation of the rapid reversibility of rheumatoid arthritis and acute rheumatic fever. The diseases which are favorably modified by cortisone and pituitary adrenocorticotropic hormone are not, however, cured by them. What is intriguing about these hormonal substances is their capability of inducing a wide variety of physiological or pharmacologic alterations. Some of these alterations, as Sprague points out, may have favorable therapeutic implications, others are relatively unimportant, while still others represent definite hazard for the patient. The extent to which the undesirable physiological effects of these hormonal agents will limit their usefulness remains to be determined by future clinical investigations.

ANNUAL CONGRESS ON MEDICAL EDUCATION AND LICENSURE

Elsewhere in this issue appears the program for the forty-seventh Annual Congress on Medical Education and Licensure to be held at the Palmer House, Chicago, February 11-13, under the sponsorship of the Council on Medical Education and Hospitals. With the impact of the current emergency and mobilization uppermost today in the minds of medical educators, arrangements have been made to devote one session of the Congress entirely to a discussion of problems relating to the present crisis as they affect the medical schools and teaching hospitals. Papers outlining the present policies of the Selective Service System and the National Security Resources Board will be followed by a panel discussion of those problems that are of most concern to the medical schools. Representatives of the government services, the medical schools and civilian medicine will participate in the panel. Another feature of this portion of the program will be the report by the Joint Committee on Medical Education in Time of National Emergency of its recommendations with respect to the medical curriculum during the present crisis and its possible sequelae.

Timely papers and discussions have also been scheduled for the other sessions of the Congress. Formal papers will be presented on the continuing evolution of the medical curriculum, the survey of medical education, the supply of physicians' services, current campaigns against quackery and a newly proposed plan for the handling of internship appointments.

At another session the comparative merits of the pyramidal and vertical plans for the training of residents will be the subject of a round-table discussion. The program will be concluded by a series of papers exploring the possibility of utilizing some of the newer technics of conducting examinations in the examinations for licensure offered by the state boards of medical examiners and the National Board of Medical Examiners.

A special block of rooms is being held at the Palmer House for those planning to attend the Congress. Reservations should be made directly with the hotel at the earliest possible date.

ORGANIZATION SECTION

Questions and Answers on Registration

On Monday, January 15, physicians, dentists and veterinarians will complete their registration under Public Law 779, the "doctor draft." Major Gen. Lewis Hershey, director of Selective Service, estimates that 210,000 in the three groups will register. Under the law, passed early last fall, the President may require the registration of "allied categories" of specialists, as well as physicians, dentists and veterinarians, but so far has not called on the other groups to sign up for possible military service.

The first registration, on October 16, took in 21,000 men in priorities 1 and 2 under the draft, defined by General Hershey as "men who received training by the Army or Navy at government expense or were deferred to complete their training and who served less than 21 months subsequent to completion or release from the training program."

The following questions and answers set forth essential information for physicians concerning registration for January 15:

Who must register?

All physicians ". . . who have not reached their fiftieth birthday, except members of the regular or reserve components of the uniformed services and certain categories of aliens . . . unless they are registered under the Oct. 16, 1950 registration."

Where should a physician register?

Before a duly designated registration official or Selective Service local board having jurisdiction in the area in which he has his permanent home or in which he may happen to be on that day.

What about physical disabilities?

There is no exemption from registration because of physical disabilities; the fitness of the registrant for service will be determined at a later date.

What questions will be asked?

National Selective Service Headquarters announces that, unlike the October 16 registration, this time registrants will not be asked whether they wish to apply for reserve commissions, nor will they be asked to fill out the standard Selective Service questionnaire. However, the regular Selective Service registration card will be used. It calls for such information as:

Name, place of residence, mailing address, name and address of person who will always know the registrant's address, date and place of birth.

Occupation (or profession), firm or individual by whom employed (hospital or school), particular service rendered, place of employment (or office where registrant practices), marital status.

Local board with which registrant registered if covered by Selective Training and Service Act of 1940, whether he ever was rejected for service in the armed forces, active duty if any in the armed forces since Sept. 16, 1940.

May I join the reserves?

Yes, if qualified and acceptable to the Army, Navy or Air Force. If the registrant joins the reserves, he will be subject to military orders and Selective Service will cease processing him. The registrant will have to make special application to the particular service for a commission if he so desires.

If I do not join the reserves and am inducted, will I get a commission?

Application may be made for a commission after induction, but the registrant will not be eligible for the $100 monthly pay bonus given to medical volunteers.

Must women physicians register?

No. The registration is restricted to men.

When may I expect to be called?

For the next few months, October 16 registrants will meet most of the requirements, either as reserves or inductees. When and if it is necessary to call up men from this January 15 registration, the amount of previous military service will be a factor in deferment, as will the essential or nonessential nature of your practice or position.

Who advises draft boards regarding physicians?

Once registered, the physician's case is in the hands of his local Selective Service board, which will be guided by the law and the local, state, and national advisory committees. These committees, made up of physicians, dentists and allied personnel, were created under the draft law to advise Selective Service boards on deferment. If the local committee decides the registrant should be deferred, it will so inform the draft board.

What aliens are exempt from registering?

"Generally speaking," General Hershey explained, "those aliens are exempt from registration who have not declared their intention of becoming citizens and who fall within one of the following groups: aliens admitted for the purpose of study under . . . the Immigration Act; officials or employees of foreign governments and their families; officials or employees of public international organizations and their families; aliens connected with the United Nations Organizations; aliens who are nationals of a country with which there is in effect a treaty or international agreement exempting its nationals from military service while they are in the United States; temporary visitors in the United States."

Abstract of Minutes of Meetings of Board of Trustees Held in Cleveland During the Clinical Session of the Association, Dec. 3-7, 1950

Committee on Cosmetics.—By action of the Board the membership of the Committee on Cosmetics was increased from seven to nine, Dr. Irvin Blank, research associate in dermatology at Harvard Medical School, and Dr. Robert A. Kehoe, professor of industrial medicine, University of Cincinnati College of Medicine, being added to the Committee, and the terms of service of the members were fixed as follows: Dr. Howard T. Behrman, Dr. Morris Fishbein and Dr. A. J. Lehman to Jan. 1, 1952; Dr. Harry Foerster, Dr. Harry Huber and Dr. H. Rattner to Jan. 1, 1953, and Dr. Louis Zopf, Dr. R. A. Kehoe and Dr. Irvin Blank to Jan. 1, 1954.

State Journal Advertising Bureau.—Dr. L. Fernald Foster of Bay City, Mich., was elected to succeed himself on the Advisory Committee to the State Journal Advertising Bureau for a period of five years.

Appointments.—The Board selected Dr. James R. Reuling to represent the American Medical Association at the Diamond Jubilee meeting of the American Chemical Society to be held Sept. 3-7, 1951, in New York; Dr. Joseph Lawrence to act as the representative of the American Medical Association at the dinner to be held on December 12 in Washington to pay tribute to the Library of Congress, to which representatives of the library world and the world of learning were to gather to extend homage for the accomplishments of the past and their hopes for the future, and Dr. Russell H. Morgan to represent the Association on the committee to be appointed by the Director of the National Bureau of Standards which will prepare a safety code for the industrial use of roentgen rays and gamma rays for other than medical purposes.

Dr. E. S. Hamilton and Dr. Gunnar Gundersen were appointed as delegates to the meeting of the World Medical Association which will be held in Stockholm in September 1951, and Dr. Austin Smith, as alternate.

The following appointments were made to various editorial boards, councils and committees (unless otherwise specified, the appointee is to succeed himself): *American Journal of Diseases of Children:* Dr. J. L. Wilson; Dr. Samuel Z. Levine, New York, to succeed Dr. Oscar Schloss (resigned), and Dr. Roger L. J. Kennedy, Rochester, Minn., to succeed Dr. H. F. Helmholz (resigned). *Archives of Dermatology and Syphilology:* Dr. Paul A. O'Leary. *Archives of Internal Medicine:* Dr. Arthur Bloomfield. *Archives of Neurology and Psychiatry:* Dr. C. D. Aring, and Dr. Harold G. Wolff, New York, to succeed Dr. Louis Casamajor. *Archives of Ophthalmology:* Dr. W. L. Benedict. *Archives of Otolaryngology:* Dr. Chevalier Jackson; Dr. Robert L. Goodale, and Dr. John D. Kernan, New York, to succeed Dr. Westley M. Hunt (deceased). *Archives of Pathology:* Dr. S. B. Wolbach, Dr. W. D. Forbus, and Dr. Charles E. Dunlap, New Orleans, an additional member. *Archives of Surgery:* Dr. Waltman Walters and Dr. Barnes Woodhall. Council on Physical Medicine and Rehabilitation: Dr. Derrick Vail, Dr. W. W. Coblentz, Dr. Walter J. Zeiter, Dr. W. E. Grove and Dr. Arthur L. Watkins, Boston. Council on Pharmacy and Chemistry: Dr. Isaac Starr, Dr. Torald Sollmann and Dr. Joseph Hayman. Council on Foods and Nutrition: Dr. J. S. McLester, Dr. Russell M. Wilder, Dr. Howard B. Lewis, and Dr. Clement A. Smith, Boston, an additional member. Council on Industrial Health: Dr. Robert A. Kehoe, and Dr. Lloyd E. Hamlin, Chicago, to succeed Dr. Paul B. Magnuson. Committee for the Protection of Medical Research: Dr. L. H. Weed, Dr. Michael DeBakey and Dr. Sidney Farber.

The terms of service of the members of the Editorial Board of the Archives of Industrial Hygiene and Occupational Medicine also were established.

Dr. Francis J. Gerty of Chicago and Dr. Richard Ford of Boston were appointed to the Committee on Medicolegal Problems.

Dr. A. F. R. Andresen, Brooklyn, was selected to replace Dr. W. W. Bauer on the Professional Education Committee of the American Cancer Society.

Committee on Research.—Dr. Paul Wermer, Assistant Secretary of the Council on Pharmacy and Chemistry, has been appointed to serve also as Secretary of the Committee on Research to replace Dr. Walton Van Winkle Jr. (resigned).

Sending of Publications of Association to Japan.—Authorization was given by the Board to continue sending the publications of the Association to the Japan Medical Association for another year, in accordance with the request of that association.

Student A.M.A.—The employment of Mr. Leo E. Brown, who has been public relations director of the Medical Society of the State of Pennsylvania, for the position of executive secretary of the Student A.M.A. was approved by the Board.

M.D.—The U. S. Doctor.—The Board deemed it advisable to have as wide distribution of the film "M.D.—The U. S. Doctor" as possible and authorized the Secretary and General Manager to write to each state medical society offering a copy of the film if it will agree to use it.

The Board, on request of Mr. Louis de Rochemont, granted the rights on 16 mm. versions of films "M.D.—The U. S. Doctor" and "Here's Health" to the Department of State for foreign nontheatrical distribution through the Voice of America program.

Fund for Medical Education.—Authorization was given for the setting up of a nonprofit corporation to receive contributions for a fund for medical education, the name of the corporation to be announced in THE JOURNAL.

Officers of The Student American Medical Association

Seated (left to right): Donald Brugger, Ohio State (member of the Council), Harry W. Sandberg, Illinois (vice president), Warren R. Mullen, Michigan (president) and David Buchanan, South Dakota (treasurer). Standing (left to right): William Davenport, Arkansas; Charles Wilson, Texas; Howard Christian, Tufts; J. Allan Henderson, Oregon, and Herbert Sperling, Boston, all members of the Council. John W. Looper of Georgia (not pictured) is also a Council member.

FORTY-SEVENTH ANNUAL CONGRESS ON MEDICAL EDUCATION AND LICENSURE

Palmer House, Chicago, Feb. 11, 12 and 13, 1951

TENTATIVE PROGRAM

ADVISORY BOARD FOR MEDICAL SPECIALTIES

Sunday Morning, February 11, 9:30 A. M.—12:30 P. M.

Crystal Room

ROUND-TABLE DISCUSSION: THE PYRAMIDAL VERSUS THE VERTICAL PLAN OF RESIDENCY TRAINING

Participants to be announced.

ROUND-TABLE DISCUSSION: THE FUTURE ROLE OF THE ADVISORY BOARD FOR MEDICAL SPECIALTIES

Participants to be announced.

COUNCIL ON MEDICAL EDUCATION AND HOSPITALS, AMERICAN MEDICAL ASSOCIATION

Monday Morning, February 12, 10:00 A. M.

Red Lacquer Room

H. G. WEISKOTTEN, M.D., *Presiding*

MEDICINE, MOBILIZATION AND MANPOWER.

Howard A. Rusk, M.D., Chairman, Health Resources Advisory Committee to the National Security Resources Board and the National Advisory Committee on the Selection of Doctors, Dentists and Allied Specialists to the Selective Service System.

CLASSIFICATION POLICIES OF THE SELECTIVE SERVICE SYSTEM.

Col. Richard H. Eanes, M.D., Chief Medical Officer, Selective Service System.

RECOMMENDATION REGARDING THE CURRICULUM DURING TIME OF NATIONAL EMERGENCY: REPORT OF JOINT COMMITTEE ON MEDICAL EDUCATION IN TIME OF NATIONAL EMERGENCY.

Stanley W. Olson, M.D., Dean, University of Illinois College of Medicine, Chairman, Subcommittee on Curriculum.

PANEL DISCUSSION: PROBLEMS ARISING FROM MOBILIZATION.

Victor Johnson, M.D., Moderator, Director, Mayo Foundation for Medical Education and Research.

Howard A. Rusk, M.D.

Col. Richard H. Eanes, M.D.

Stanley W. Olson, M.D.

Richard L. Meiling, M.D., Director of Medical Services, Office of Secretary of Defense.

Brig. Gen. Paul R. Robinson, M.D., Chief, Personnel Division, Office of the Surgeon General, United States Army.

Brig. Gen. Dan C. Ogle, M.D., Deputy Surgeon General, United States Air Force.

Rear Admiral A. H. Dearing, M.D., Assistant Chief of Bureau for Personnel and Professional Operations, Bureau of Medicine and Surgery, United States Navy.

W. Palmer Dearing, M.D., Deputy Surgeon General, Public Health Service.

E. H. Cushing, M.D., Assistant Medical Director for Research and Education, Veterans Administration.

Paul Barton, M.D., Executive Secretary, National Advisory Committee on the Selection of Doctors, Dentists and Allied Specialists to the Selective Service System.

Harold Diehl, M.D., Dean, University of Minnesota Medical School.

Stockton Kimball, M.D., Chairman, Joint Committee on Medical Education in Time of National Emergency.

Donald G. Anderson, M.D., Secretary, Joint Committee on Medical Education in Time of National Emergency.

Monday Afternoon, February 12, 2:15 P. M.

ADDRESS OF THE CHAIRMAN: THE CONTINUING EVOLUTION OF THE MEDICAL CURRICULUM.

H. G. Weiskotten, M.D., Chairman, Council on Medical Education and Hospitals, American Medical Association.

SURVEY OF MEDICAL EDUCATION: METHODS OF STUDYING THE ACTIVITIES OF MEDICAL SCHOOLS.

John E. Deitrick, M.D., Director, Survey of Medical Education.

SURVEY OF MEDICAL EDUCATION: A PROGRESS REPORT FROM THE SUBCOMMITTEE ON PREPROFESSIONAL EDUCATION.

Aura Severinghaus, Ph.D., Chairman.

Harry J. Carman, Ph.D., Director of Study.

THE STUDENT AMERICAN MEDICAL ASSOCIATION.

Warren Mullen, University of Michigan Medical School, President, Student American Medical Association.

PLAN FOR ARRANGING INTERNSHIP APPOINTMENTS BY MATCHING THE PREFERENCES OF STUDENTS AND HOSPITALS.

F. J. Mullin, Ph.D., Chairman, National Inter-Association Committee on Internships.

Monday Afternoon, 5:00 P. M.

Room Fourteen

RECEPTION FOR REGISTRANTS OF THE CONGRESS BY THE AMERICAN MEDICAL ASSOCIATION

THE FEDERATION OF STATE MEDICAL BOARDS OF THE UNITED STATES

Monday Evening, February 12, 7:00 P. M.

FEDERATION DINNER

Crystal Room

Speaker and subject to be announced.

Tuesday Morning, February 13, 9:30 A. M.

Red Lacquer Room

CREIGHTON BARKER, M.D., *Presiding*

ADDRESS OF THE PRESIDENT.

Creighton Barker, M.D., President, Federation of State Medical Boards of the United States.

RESETTLEMENT OF DISPLACED PHYSICIANS: A NEW APPROACH.

James Brunot, Executive Secretary, National Committee for Resettlement of Displaced Professionals, Inc.

SUPPLY OF PHYSICIANS' SERVICES.

Frank G. Dickinson, Ph.D., Director, Bureau of Economic Research, American Medical Association.

CURRENT CAMPAIGNS AGAINST MEDICAL QUACKERY.

Oliver Field, Director, Bureau of Investigation, American Medical Association.

Tuesday, 12:00 Noon

Room Nine

FEDERATION LUNCHEON

Tuesday Afternoon, 2:00 P. M.

Red Lacquer Room

PANEL DISCUSSION: THE OBJECTIVE OR MULTIPLE CHOICE TYPE OF EXAMINATION.

Creighton Barker, M.D., Moderator.

PRINCIPLE AND PURPOSE.

Lillian D. Long, Ph.D., Director, Merit System Service, American Public Health Association.

USE IN MEDICAL SCHOOLS.

John M. Stalnaker, Director of Studies, Association of American Medical Colleges.

NATIONAL BOARD OF MEDICAL EXAMINERS.

John P. Hubbard, M.D., Associate Secretary, National Board of Medical Examiners.

AMERICAN BOARD OF PREVENTIVE MEDICINE AND PUBLIC HEALTH.

Ernest L. Stebbins, M.D., Secretary, American Board of Preventive Medicine and Public Health.

AMERICAN BOARD OF INTERNAL MEDICINE.

Victor W. Logan, M.D., Librarian, American Board of Internal Medicine.

STATE LICENSURE EXAMINATIONS.

Walter L. Bierring, M.D., Secretary, Federation of State Medical Boards of the United States.

Tuesday Afternoon, 4:15 P. M.

Red Lacquer Room

BUSINESS SESSION—ELECTION OF OFFICERS.

MEDICAL NEWS

ARKANSAS

Army Officers on Teaching Staff.—The School of Medicine of the University of Arkansas at Fayetteville has appointed two Army medical officers to its teaching staff. The officers are Col. Charles T. Young (MC) and Col. William W. Nichol (MC), both assigned to the Army and Navy General Hospital, Hot Springs National Park. Colonel Young has been appointed assistant professor of medicine, and Colonel Nichol was named associate professor of surgery.

Annual Neuropsychiatric Meeting.—The third annual neuropsychiatric meeting will be held at the Veterans Administration Hospital, North Little Rock, March 1-2. Many former staff members are expected to return for the occasion. Speakers include Drs. Harold G. Wolff, New York; Jules H. Masserman, Chicago; Edwin F. Gildea, St. Louis; Saul Rosenzweig, Detroit; Harvey J. Tompkins, Washington, D. C.; Edward D. Greenwood, Topeka, Kan.; Dr. Crawford N. Baganz, Lyons, N. J.; Miss Elizabeth S. Bixler, dean, Yale University School of Nursing, New Haven, Conn., and The Rev. Harold Wilke, Chicago. There will be many professional exhibits and clinical demonstrations having to do with the hospital and its diagnostic and therapeutic activities. A special conference for nurses will be held on February 28, and psychologists and social workers will have sessions at regular intervals during the meeting. There is no charge for registration, and attendance of all interested professional personnel will be welcomed. Information may be obtained from Dr. Ewin S. Chappell, director of professional education, Veterans Administration Hospital, North Little Rock.

ILLINOIS

Award for Paper by Psychiatric Resident.—The Illinois Psychiatric Society will award $200 to the psychiatric resident presenting the most original paper on a psychiatric research problem. The author of the paper must be a resident physician in training at an approved psychiatric facility or institute in Illinois. Papers should be sent to the chairman of the Award Committee, Dr. Clarence A. Neymann, 104 South Michigan Avenue, Chicago, by February 28. The prize paper will be presented before the Illinois Psychiatric Society at its April meeting.

Chicago

Society News.—The Institute of Medicine of Chicago announces the following officers for 1951: Dr. Walter H. Theobald, president; Charles W. Freeman, D.D.S., vice president; Dr. George H. Coleman, secretary, and Dr. E. Lee Strohl, treasurer. Dr. Henry T. Ricketts has been reelected chairman of the board of governors.

Hektoen Institute Appointments.—At the annual meeting of the Board of Trustees of the Hektoen Institute for Medical Research, held on December 14, Dr. Edmund F. Foley, Ross D. Siragusa and Jack Galter were appointed members of the board of trustees, and Drs. Benjamin M. Gasul, Morton I. Grossman, Abraham Levinson and William H. Shlaes, research associates.

Dr. Menninger to Give Oppenheim Lecture.—Dr. Karl Menninger, director of the Menninger Clinic, Topeka, Kan., will speak on "Psychiatry and Medicine" at the second annual Maurice Oppenheim Memorial Lectureship sponsored by Alpha Rho Chapter, Phi Lambda Kappa of the Chicago Medical School. The lecture will be held at 12: 15 p. m. in the Kling Auditorium of Mount Sinai Hospital January 24.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education and public health. Programs should be received at least two weeks before the date of meeting.

Promotions at Illinois.—The University of Illinois College of Medicine has announced the promotion of the following persons from the rank of clinical assistant professor to clinical associate professor: Drs. Stuyvesant Butler and Alva A. Knight in medicine, Dr. Frank G. Murphy in orthopedic surgery and Dr. Stanley E. Lawton in surgery. Dr. Edward A. Piszcek was promoted from assistant professor to associate professor in public health.

Graduate Fellowships Open at Illinois.—Ten fellowships supported by the Graduate College of the University of Illinois will be awarded to qualified scholars who contemplate academic careers in the medical and allied sciences. Stipends of $1,800 to $2,400 are available for medical and dental graduates with a maximum of $3,000 for unusually well qualified applicants. Pharmacy graduates receive a $1,200 stipend for the calendar year. Exemption from tuition fees is provided for all appointees. Registration for work toward M.S. or Ph.D. degrees is required. Applicants need not have completed clinical internships. Minimum requirements are Bachelor and M.D. degrees; Bachelor and D.D.S. degrees; Bachelor degree in pharmacy and M.S. degree. The fellowships provide an opportunity for research experience in the basic sciences and the application of these sciences to clinical investigation. Applications must be received by February 15, with selections to be announced by April 1. Forms may be obtained from the associate dean of the Graduate College, University of Illinois, 808 South Wood Street, Chicago 12.

INDIANA

Dr. Conlin to Address Conference.—Dr. John F. Conlin of Boston, director of medical information and education of the Massachusetts Medical Society, will address the annual Conference of County Medical Society Officers at Indianapolis on January 28 on "The Role of the Individual Physician in His Community." Dr. Albert M. Mitchell of Terre Haute, chairman of the conference, will preside.

KENTUCKY

Infectious Hepatitis.—The Kentucky State Department of Health recently reported to the U. S. Public Health Service two outbreaks of infectious hepatitis in two widely separated areas of the state in one week. Only children were affected.

Director of Tuberculosis Control.—Col. Paul M. Crawford, former chief surgeon at Fort Knox who retired in October, has been appointed director of tuberculosis control for the state department of health, a position that has been vacant for two years. From 1925 to 1929 he worked closely with tuberculosis patients at Gorgas Hospital at Ancon, in the Canal Zone. Later he was assistant chief of medical service at Fitzsimons General Hospital, Denver. In World War I he served overseas with the Seventh Infantry Division and in World War II was in command of the Second General Hospital in England and France.

LOUISIANA

Dr. Lahey to Give the Matas Lecture.—The Beta Iota Chapter of the Nu Sigma Nu Fraternity announces the annual Rudolph Matas Lecture, to be given at 8: 00 p. m. February 9 at Dixon Hall, Tulane University of Louisiana School of Medicine, New Orleans. The guest lecturer will be Dr. Frank Lahey of the Lahey Clinic, Boston. Members of the profession are invited.

Psychiatric Fellowships Awarded.—Four young New Orleans physicians are the recipients of the first Farnsworth fellowships in psychiatry, established last year to bolster the staffs of Louisiana mental hospitals. The program, established by R. P. Farnsworth and Co., Inc., is sponsored at the Louisiana Society for Mental Health. The recipients are Drs. William R. Sorum,

Andre A. Charles L. Touzet, Frederick R. Hine and George W. Burke. Each will receive a grant of $3,000 to be paid during a three year hospital residency, with the understanding that at the end of the residency he will spend at least one year on the staff of a Louisiana mental hospital. A special committee of the society, who made the selections, includes Dr. Henry O. Colomb, Robert G. Heath and Robert A. Matthews, Mr. Jesse H. Bankston and Lloyd W. Rowland, Ph.D., all of New Orleans.

MASSACHUSETTS

Grant for Public Health Training.—A five year grant totaling $141,712 has been awarded the Massachusetts Department of Public Health by the Kellogg Foundation of Michigan. The fund will be used to enlarge the recently created New England Field Training Center to include the training of physicians, nurses, medical social workers, health educators, administrators and others in public health work. Located at the University of Massachusetts, Amherst, the training center is co-sponsored by the Communicable Disease Center of U. S. Public Health Service, the state health department and the university. Appointed as director of the training program is Leon A. Bradley, Ph.D., of Amherst, former head of the University of Massachusetts' department of bacteriology and public health. Dr. Bradley also is president of the Massachusetts Public Health Association. The $141,700 grant will be used also to enable personnel to obtain field training in certain local health departments throughout the state.

At present the residents of at least 95 per cent of Bay State towns are failing to receive adequate protective health services. To relieve the situation the health law passed in 1949 makes it compulsory for communities of less than 35,000 population to combine into full time health unions within 10 years. Based on population figures, some 40 full time local health departments are needed throughout the state to provide all residents with minimum health services. To staff the new health unions will require the training of scores of new professional workers.

MICHIGAN

Cerebral Palsy Clinics.—Dr. Meyer A. Perlstein, Chicago, will hold cerebral palsy clinics in Battle Creek January 29-30 and in Kalamazoo January 31-February 1. He will be in Lansing February 26-27 and in Jackson February 28-March 1.

Personal.—The National Research Council, Division of Medical Sciences, Washington, D. C., has named Walter H. Seegers, Ph.D., of Wayne University College of Medicine, Detroit, as chairman of the subcommittee on the chemistry of blood coagulation. Dr. Seegers, who is chairman of Wayne's department of physiology, has been engaged for four years in blood coagulation research, aided by grants from the National Institutes of Health.

Eye Institute and Wayne University Affiliate.—Formal affiliation of the Kresge Eye Institute with the Wayne University College of Medicine was approved by the Detroit Board of Education December 26. Appointments to the scientific staff of the institute will be made by the board of trustees of the institute when such recommendations bear the endorsement of the faculty of the Wayne University College of Medicine. In addition, the dean of the college of medicine, or his appointed representative, will be a member of the board of trustees, and the director of the institute, or his appointed representative, will be a member of the committee on administration of the college of medicine.

MINNESOTA

The Eighteenth Judd Lecture.—The eighteenth E. Starr Judd Lecture will be given by Dr. Emile F. Holman, professor of surgery, Stanford University School of Medicine, San Francisco, February 15, at 8: 15 p. m. in the Amphitheater, Medical Sciences at the University of Minnesota, Minneapolis. The subject will be "Surgical Treatment of Constrictive Pericarditis: Clinical and Experimental Observations." Dr. E. Starr Judd, an alumnus of the University of Minnesota Medical School, established this annual lectureship in surgery a few years before his death.

NEW YORK

Personal.—Dr. Robert H. Broh-Kahn has been named medical director of Bristol Laboratories, Inc., Syracuse. Dr. Broh-Kahn was formerly assistant director of the May Institute for Medical Research, Cincinnati. He was an instructor in bacteriology at the College of Medicine in Cincinnati from 1941 to 1948. During the past two years he has also been assistant professor of experimental medicine at the University of Cincinnati.

Psychoanalytic Training Center.—Training in psychoanalytic medicine is now being given at the College of Medicine of the State University of New York in New York City. Dr. Howard W. Potter, professor of psychiatry, has set up within the department a division of psychoanalytic medicine. Dr. Sandor Lorand has been appointed chairman of the executive committee of this division. Candidates for training are appointed from among graduates of the psychiatric residency program, from psychiatric residents in advanced standing and from members of the staff of the college and its affiliated hospitals.

New York City

Hospital News.—Ground breaking ceremonies for the Long Island Jewish Hospital were held December 10. It is being built on the Queens-Nassau border at 263d Street and 76th Avenue, Bellerose, by the Federation of Jewish Philanthropies of New York. The hospital will provide 200 beds in wards and private and semiprivate facilities, serving residents of Queens and Long Island on a nonsectarian basis.

Fifth Harvey Lecture.—Dr. John Runnström, professor of experimental zoology at the Faculty of Science of the University of Stockholm and director of the Wenner-Gren Institute for Experimental Biology, Stockholm, Sweden, will deliver the Fifth Harvey Lecture of the current series at the New York Academy of Medicine on January 18 on "The Problem of Fertilization as Elucidated by Experiments on Sea Urchins."

Open Unit of Medical Center.—Dedication ceremonies marking the opening of New York University-Bellevue Medical Center's Institute of Physical Medicine and Rehabilitation will be held January 24. The center's first new unit, located at 400 East Thirty-Fourth Street, is being completed at a cost of $2,055,000. The new facilities will provide for 80 inpatients and 150 outpatients per day, more than doubling the present capacity for service. The center's new unit is a four story building.

Medical Service for Low Income Families.—State and city housing officials and Mount Sinai Hospital have set up plans for a voluntary hospital service for "family doctor" service and preventive medicine. Beginning in 1952, medical, psychiatric and dental care will be provided for 400 of the 1,200 low income families that occupy Carver Houses on Madison at 100th Street and 100 families of similar "medical indigence" from surrounding tenements. Families will be instructed in proper hygiene, sanitary and dietary habits. The "outpost" will be a hospital extension of 1,200 square feet in Carver Houses, which will be built with funds borrowed from the state and in part from the housing authorities. Mount Sinai Hospital has allocated $5,000 toward administrative costs, estimated at $60,000 a year. The hospital will assign staff physicians to part time work at the extension. Services are to include minor ambulant care, prenatal, a well-baby clinic, dental care for children, nutrition guidance, sanitation, preventive services, group health education, psychological guidance, psychotherapy where indicated and annual family health inventory.

Special Lecture Series on Atomic Medicine and Medical Developments.—The city department of health has arranged for physicians a special series of four lectures on "Medical Aspects of Atomic Explosion" and a series of 13 meetings on "New Developments in Medical Diagnosis and Treatment," the latter especially for general practitioners. Meetings are on consecutive Saturday mornings from 10: 30 a. m. to 11: 30 a. m. at the department of health, 125 Worth Street, Manhattan. No fee is required. Physicians who attend can be reached by their offices at Worth 2-6900, extension 252.

MEDICAL ASPECTS OF ATOMIC EXPLOSION

Jan. 6, Jacob H. Landes, New York City Department of Health, Elementary Nuclear Physics.
Jan. 13, Morris A. Jacobs, New York City Office of Civil Defense, Emergency Plan for Medical Mobilization.
Jan. 20, Borris A. Kornblith, Gouverneur Hospital, Treatment of Mechanical and Thermal Injuries.

NEW DEVELOPMENTS IN MEDICAL DIAGNOSIS AND TREATMENT

Feb. 3, Arthur B. Robins, director, Bureau of Tuberculosis, Modern Attack Against Tuberculosis.
Feb. 10, Howard B. Shookhoff, Tropical Disease Diagnostic Service, New York City Department of Health, Occurrence and Treatment of Parasitic Diseases in New York City.
Feb. 17, Emanuel Appelbaum, Bureau of Laboratories, Treatment of Meningitis.
Feb. 24, Norman H. Jolliffe, Director, Bureau of Nutrition, Clinical Diagnosis of Nutritional Deficiencies.
March 3, Robert B. McGraw, Columbia University College of Physicians and Surgeons, Psychosomatic Medicine for the General Practitioner.
March 10, Yale Kneeland Jr., Columbia University College of Physicians and Surgeons, Clinical Use of Antibiotics.
March 17, Nathan Sobel, New York University College of Medicine, Differential Diagnosis of Cutaneous Syphilis.
March 24, Alexander B. Gutman, First Goldwater Memorial Hospital, Hypertensive Vascular Disease.
March 31, Samuel C. Miller, D.D.S., Dental Problems for the General Practitioner.
April 7, Bernard S. Wolf, Mount Sinai Hospital, Radio-Isotopes in Medicine.
April 14, Sidney C. Werner, Columbia University College of Physicians and Surgeons, Therapy of Endocrine Disorders.
April 21, Irving S. Wright, Use and Abuse of Anticoagulant Drugs.
April 28, Frederick D. Zeman, Chronic Diseases in Old Persons.

PENNSYLVANIA

Ophthalmologic Meeting.—Dr. Arthur A. Knapp will speak at a meeting of the Wilkes-Barre Ophthalmological Society on January 30 on "Criteria for Surgical Decision" and will show a movie of "Tattooing with Iridectomy."

Personals.—Dr. Yale D. Koskoff has been appointed director of research and medical and surgical services at the Montefiore Hospital, Pittsburgh.——Dr. William L. Estes Jr., of Bethlehem, a former president of the Medical Society of the State of Pennsylvania, has been named chairman of the Board of Governors of the American College of Surgeons.——Dr. Leroy E. Chapman was entertained at a testimonial dinner December 12 given in Warren by the Warren County Medical Society. Dr. Chapman was cited for his lifetime service to the community and for representing the medical profession in the state senate for five terms.

Philadelphia

Personal.—Dr. Joseph Seifter, director of research at the Wyeth Institute of Applied Biochemistry since 1947, was elected in December to fellowship in the New York Academy of Sciences.

A. O. A. Chapter at Temple.—The Epsilon Chapter of Pennsylvania, Alpha Omega Alpha, honorary medical society, was installed at the Temple University School of Medicine, Philadelphia, on December 1. The charter was conferred by Dr. Walter L. Bierring, Des Moines, Iowa, national president, and was accepted by Robert L. Johnson, LL.D., president, Temple University. The installation address was made by Dr. Wilburt C. Davison, dean, Duke University School of Medicine, Durham, N. C.

Hospital's Two Hundredth Anniversary.—In 1951 Pennsylvania Hospital, Philadelphia, will observe the beginning of its third century as the nation's first hospital. The occasion also marks the two hundredth anniversary of the voluntary hospital system in this country. Pennsylvania Hospital was founded, largely through the efforts of Benjamin Franklin and Dr. Thomas Bond, by act of the Colonial Assembly on May 11, 1751, primarily as the charter states, for "relief of the sick poor and for the reception and cure of lunaticks." Prior to that time there had been only an almshouse, which, however, could not be called a hospital as such. In its beginning the hospital had only three regularly attending physicians, four consultants, a matron to care for the house and twenty-three patients. Today its two major departments, the department for the sick and injured and the department for mental and nervous diseases, together handle 21,000 annual admissions, and their outpatient clinics record some 151,000 visits by ambulant patients each year. Personnel, including medical, administrative and other employees, number more than 970. Pennsylvania hospital performs $800,000 to $900,000 of charitable work annually, made possible primarily through the generosity of contributors who have made grants to the hospital during their lifetimes and in their wills.

Pittsburgh

Society News.—The next meeting of the Pittsburgh Otological Society will be held February 1, at the Pittsburgh Athletic Association. Dr. French K. Hansel, director of the Hansel Foundation, St. Louis, will discuss "Allergy in Otolaryngology."

University Appointment.—Harwood S. Belding, Ph.D., has been appointed professor of environmental physiology at the University of Pittsburgh Graduate School of Public Health. Dr. Belding has since 1946 been director of the Quartermaster Climatic Research Laboratory, Lawrence, Mass.

TEXAS

Truett Hospital Dedicated.—The $5,500,000 eight-floor George W. Truett Hospital was formally opened November 30 in Dallas. The 436 bed building, newest addition to Baylor University Hospital, makes Baylor an 850 bed institution. A bronze bust of Dr. Truett, First Baptist Church pastor who died in 1934, was unveiled at the dedication. The university and civic leaders and representatives of the Baptist General Convention took part in the ceremonies.

Personals.—Dr. Harvey C. Slocum, Galveston, has been elected a director of the American Board of Anesthesiology succeeding Dr. John W. Winter of San Antonio.——Col. Robert K. Simpson (USA, retired), of Kerrville, on December 2 was presented the Military Merit Medal of the Commonwealth of the Philippines by Lieut. Col. Pelagio G. Potenciano, Air Surgeon, Philippine Air Force. The award was for services rendered in 1937 and 1945, when Colonel Simpson was able to train 14 Philippine medical officers as aviation medical examiners and was instrumental in having two Philippine medical officers attend Air Corps training centers in the United States. He was able also to facilitate the sending of six Philippine nurses to the United States for specialized training.

VIRGINIA

Dr. Truslow Becomes Dean.—Dr. John B. Truslow, assistant dean at Columbia University College of Physicians and Surgeons, New York, became dean of the Medical College of Virginia, Richmond, on January 1, succeeding Dr. Harvey B. Haag, who recently resigned to give full time to research and to teaching in pharmacology. Dr. Truslow has been dean at Columbia since 1946, prior to which he served with the U. S. Navy for five years.

WISCONSIN

Lecture on Nutrition.—The Medical School Society of the University of Wisconsin on February 6 will present a lecture on "The Problem of Intravenous Nutrition" by Dr. Paul R. Cannon, chairman of the department of pathology at the University of Chicago, The School of Medicine. The lecture will be held at 8: 00 p. m. in the auditorium, Service Memorial Institutes.

GENERAL

Society Election.—The Southern Psychiatric Association, meeting in Williamsburg, Va., November 27, elected Dr. R. Burke Suitt, Durham, N. C., as president; Dr. Oscar S. Hauk, Nashville, Tenn., president-elect, and Dr. Joseph E. Barrett, Virginia's Commissioner of Mental Hygiene, Richmond, as chairman of the board of regents.

Birth Rate in 1950.—Another bumper crop of babies started life's journey in the United States during 1950. By year's end the number of births totalled nearly 3,700,000, the Metropolitan Life Insurance Company's statisticians estimated, which is only 5 per cent below the all-time high of 1947. This year was fourth in succession in which the number of births exceeded 3,500,000. The sustained high level of births is particularly remarkable since the number of marriages dropped rather sharply between 1946 and 1949. The births during 1950 were at the rate of 24 per 1,000 of the population, including the armed forces overseas.

Residencies for General Practice.—The University of Pittsburgh School of Medicine and the Medical Center Hospitals announce a new residency for the training of general practitioners to begin July 1, 1951. This residency will consist of one year of hospital and outpatient work in the Medical Center Hospitals. Eight months of training will be devoted to internal medicine, emergency surgery, obstetrics and pediatrics. The remaining four months will consist of specialty training which the resident may choose to take. Provision for a second year of residency has been made should the resident desire it. Information may be obtained from the Chairman of the Committee on Graduate Medical Education, University of Pittsburgh School of Medicine, Pittsburgh 13.

Society for Prevention of Blindness.—In the annual report of the National Society for the Prevention of Blindness, Mason H. Bigelow, president, said that the 1951 budget for the society's campaign of research education and preventive services is $423,067, an increase of $14,758 over that of 1950. One of the major statistical studies during the year, he said, was an investigation in Louisville, Ky., which indicated that about 16,000 eye accidents occurred each year among American children, in which 750 lose the sight of an eye. About 800,000 Americans have glaucoma and do not know it, he reports. Sixteen directors were elected at the meeting; Drs. William L. Benedict, Rochester, Minn.; Eugene M. Blake, New Haven, Conn.; Albert J. Chesley, St. Paul; John H. Dunnington, Leonard Greenburg, Thomas H. Johnson, James G. Mooney, Mr. Keith Lorenz, Mr. Lawrence B. Eilliman Jr., Mr. Donald H. Hoover, Mr. Carleton H. Palmer and Mr. Clifford W. Michel, all of New York; Dr. Wilton L. Halverson, San Francisco; The Rev. Alphones M. Schwitalla, St. Louis; Charles Sheard, Ph.D., Rochester, Minn., and Mr. D. Spencer Berger, New Haven, Conn.

Academy of Orthopaedic Surgeons.—The American Academy of Orthopaedic Surgeons will hold its annual meeting at the Palmer House, Chicago, January 27-February 1, under the presidency of Dr. Guy A. Caldwell, New Orleans. An audio-visual education program will be given Saturday beginning at 2: 00 p. m. and Sunday morning. Instructional courses will be held on Sunday afternoon and Monday morning. Twelve will run simultaneously. Those presenting papers by invitation on the scientific program include:

John E. Howard, Baltimore, Current Concepts on the Mechanism of Calcification.

Zachary B. Friedenberg, Philadelphia, Effect of Known Compression Forces on Fracture Healing.

Sten Friberg, Stockholm, Sweden, Anatomic and Clinical Studies on Intervertebral Disk Degeneration.

Walter Bauer, Boston, Nature of Rheumatoid Arthritis and Its Management.

August W. Spittler, Washington, D. C., Cineplastic Muscle Motors for Prostheses of Arm Amputees.

The annual banquet will be held at 7: 30 p. m. Wednesday. Both scientific and technical exhibits will be shown.

International Medical and Surgical Meetings.—The first International Show of Medical Arts and the International Medical-Surgical Meetings will take place in the Palace of Exhibitions in the Valentino Gardens of Turin, Italy, May 30 to June 12, sponsored by the Minerva Medical and the Italian Medical Associations. The show of medical arts will include the following sections: (1) social medical assistance, (2) organization of hospitals, (3) machinery connected with hospitals, (4) pharmaceutical products, (5) the mother and the child, (6) medicine and work, (7) rehabilitation and prevention of disablement, (8) hygiene and athletics, (9) instruction and publication and (10) civil and military aspects of public health. Special committees have been organized for the specialties. National and regional conferences will be held at the same time. The organization of an international meeting of manufacturers of pharmaceutical products and a meeting of international manufacturers of surgical medical instruments are also included. Prof. A. M. Dogliotti, director of the Clinica Chirurgica of Turin, is chairman of the planning committee. Further information may be obtained from the General Secretary, Prof. Stefano Teneff, Palazzo delle Esposizioni al Valentino, Torino, Italia.

Report of Crippled Children's Society.—The National Society for Crippled Children and Adults reports that it gave direct services to over 228,000 crippled children and adults during 1950, exclusive of indirect services rendered by its affiliates to thousands of other crippled persons and those who work with them. The direct services included such help as diagnostic clinics, hospitalization and convalescent care, physical, occupational and speech therapy, mobile clinics, special teaching, sheltered workshops and employment, opportunity and placement counseling, cerebral palsy treatment centers, nursery schools, camping and recreational facilities and rehabilitation centers. The cost was met primarily by the largest Easter Seal fund ever contributed by the American public, a total of about $6,000,000 augmented by special grants and bequests from organizations and individuals. The National Society and its affiliates has a nationwide cerebral palsy program, which in 1950 grew to include more than 170 facilities specifically set up to care for cerebral palsied children. The indirect services rendered by the society include public education on the problems of the crippled; education of physicians, nurses, therapists, teachers and others who serve the crippled directly; special education programs for those who live with the crippled, primarily their parents; legislative guidance to state and national legislative bodies on improved public service facilities for the crippled, and research activities designed to prevent crippling conditions where possible and to improve technics and procedures for dealing with those that cannot be prevented.

March of Dimes Research and Education Grants.—The National Foundation for Infantile Paralysis, on recommendation of its Medical Advisory Committees, recently approved $1,509,990 for the continuation of research and professional educational programs seeking the prevention of poliomyelitis, improved methods of treatment of the disease and the training of more professional persons to speed research and to provide better care for patients. The programs at universities and research centers in 16 states and Canada became effective January 1. The research projects include continuing attempts to develop an effective vaccine for poliomyelitis, search for a chemical agent that will prevent the virus from damaging nerve cells, development of a rapid diagnostic test and the preparation of an antiserum that will increase resistance to paralysis. The new grants and appropriations bring the total to over $25,000,000 in March of Dimes funds spent for research and education by the National Foundation since 1938. In addition, the foundation has spent $102,000,000 on patient care in the same period. All monies are derived from the voluntary contributions of the American people to the annual March of Dimes. Part of the funds authorized for research projects will go to the universities as payment for the "hidden costs" of conducting research. Such items include heat, light and power, building maintenance and the other charges that ordinarily are not included in a research budget but are related to the research and drain funds from the universities. In addition, funds have been authorized for the pre-

liminary investigation of emergency research projects which could not await the regular consideration of advisory committees and the board of trustees. Similarly, funds were set aside for scholarships and fellowships which are administered directly by the National Foundation.

FOREIGN

WHO Sends Leprosy Expert to Ethiopia.—The World Health Organization has assigned Dr. M. A. K. Dalmagouni, director of the Leprosy Section of the Egyptian Ministry of Health, to visit Ethiopia, which has an estimated 15,000 to 20,000 cases of leprosy. Ethiopia, WHO has pointed out, has a large leper colony outside Addis Ababa and another at Harar. Ethiopian delegates to WHO meetings have outlined social problems resulting from the disease in their country.

German Society of Internal Medicine.—The fifty-seventh meeting of the German Society of Internal Medicine will be held April 2-5 in Wiesbaden, Germany, under the chairmanship of Prof. Dr. M. Bürger of the Medical Clinic in Leipzig. The chief subjects are as follows: relations between hypophysis and adrenals, changes in the manifestations of thyroid diseases, pulmonary cancer and its treatment, the physical and biologic foundations of ultrasonic therapy and diabetes as endocrine disturbance in its relations to tuberculosis. Application for papers to be presented must be made before January 15 and must be addressed to the chairman. Applications for participation in the meeting will be accepted up to February 15 and must be sent to the Secretary of the Society, Prof. Dr. Fr. Kauffmann (16) Wiesbaden, Germany, Städt. Krankenanstalten.

DEATHS IN OTHER COUNTRIES

Dr. James A. Murray, pioneer in experimental cancer research who for 32 years worked in the laboratories of the Imperial Cancer Research Fund and for the last 20 as its director, died in Hove, England, November 20, aged 76.

CORRECTION

Sunlight and Tuberculosis.—In the answer to the query with this title in THE JOURNAL Nov. 4, 1950, page 887, in the fourth line of the answer the words "fats and lipids" should have read "cholesterol."

EXAMINATIONS AND LICENSURE

National Board of Medical Examiners

NATIONAL BOARD OF MEDICAL EXAMINERS: *Parts I and II.* Various Centers. Feb. 13-15, April 16-17 (Part II only), June 18-20, Sept. 5-7. Ex. Sec., Mr. E. S. Elwood, 225 S. 15th Street, Philadelphia.

Examining Boards in Specialties

AMERICAN BOARD OF ANESTHESIOLOGY: *Written.* July 20. Given simultaneously in several cities in the United States. Final date for filing application is Jan. 20. *Oral.* Coronado, Calif., April 4-7 and Memphis, Oct. 14-17. Sec., Dr. Curtiss B. Hickcox, 80 Seymour St., Hartford 15, Conn.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: *Written.* Various Centers, Feb. 8. *Oral.* New York, April 6-8. Sec., Dr. George M. Lewis, 66 East 66th St., New York 21, N. Y.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: *Oral.* Chicago, May 1951. Sec., Dr. W. J. German, 789 Howard Ave., New Haven 4, Conn.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: Part I, Written Examination and Review of Case Histories. Various locations. Feb. 2, 1951. Final date for filing applications was Nov. 5, 1950. *Oral.* New York City, May 10-16. Final date for filing application is Feb. 2. Sec., Dr. Paul Titus, 1015 Highland Building, Pittsburgh 6, Pa.

AMERICAN BOARD OF OPHTHALMOLOGY: *Oral.* San Francisco, March 11-15; New York, May 31-June 5; Chicago, October 8-13. Sec., Dr. Edwin B. Dunphy, 56 Ivie Road, Cape Cottage, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Part II.* Chicago, Jan. 25-26. Final date for filing applications was Aug. 15, 1950. Final date for receipt of Part I applications for 1951 was Dec. 30, 1950. Sec., Dr. Harold A. Sofield, 122 S. Michigan Ave., Chicago 3.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Oral.* Richmond, Va., May 1-5. Sec., Dr. Dean M. Lierle, University Hospital, Iowa City.

AMERICAN BOARD OF PATHOLOGY: *Written and Oral. Pathological Anatomy and Clinical Pathology.* Cleveland, April 23-24. Final date for filing application is March 15. Sec., Dr. Robert A. Moore, 1402 S. Grand Blvd., St. Louis.

AMERICAN BOARD OF PEDIATRICS: *Written.* Jan. 19. Under local monitors. Only written examination to be given during 1951. *Oral.* New Orleans, March 2-4. Ex. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

AMERICAN BOARD OF PHYSICIAL MEDICINE AND REHABILITATION: *Parts I and II.* Philadelphia, June 16-17. Final date for filing application is March 31. Sec., Dr. Robert L. Bennett, 30 N. Michigan Ave., Chicago.

AMERICAN BOARD OF PROCTOLOGY: *Part I in Anorectal Surgery and Proctology.* Kansas City, Minneapolis, Philadelphia and San Francisco, May 12. Sec.-Gen., Dr. Louis A. Buie, 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: Philadelphia, June 11-12. Final date for filing application is March 1. Sec., Dr. Francis J. Braceland, 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF RADIOLOGY: *Oral.* Atlantic City, June 5-9. Sec., Dr. B. R. Kirklin, 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Written.* Various centers, March 1951. Final date for filing applications was Dec. 1, 1950. *Written.* Various centers, Oct. 1951. Final date for filing applications is July 1. Sec., Dr. J. Stewart Rodman, 225 South 15th Street, Philadelphia.

BOARD OF THORACIC SURGERY: *Written.* Various Centers, Feb. 17. Final date for filing application is Feb. 1. *Oral.* New York City, April 19. Sec., Dr. William M. Tuttle, 1151 Taylor Ave., Detroit.

AMERICAN BOARD OF UROLOGY: Chicago, Feb. 10-14, 1951. Final date for filing applications was Sept. 1, 1950. Chicago, Feb. 9-13, 1952. Final date for filing applications is Sept. 1. Sec., Dr. Harry Culver, 314 Corn Exchange Bldg., Minneapolis 15.

MEETINGS

ANNUAL CONGRESS ON INDUSTRIAL HEALTH, Atlanta Biltmore Hotel, Atlanta, Ga., Feb. 26-28. Dr. Carl M. Peterson, 535 N. Dearborn St., Chicago 10, Secretary.

ANNUAL CONGRESS ON MEDICAL EDUCATION AND LICENSURE, Palmer House, Chicago, Feb. 12-13. Dr. Donald G. Anderson, 535 N. Dearborn St., Chicago 10, Secretary.

NATIONAL CONFERENCE ON RURAL HEALTH, Peabody Hotel, Memphis, Tenn., Feb. 23-24. Dr. F. S. Crockett, 535 N. Dearborn St., Chicago 10, Chairman.

AMERICAN ACADEMY OF ALLERGY, Hotel Statler, New York, Feb. 5-7. Dr. Walter S. Burrage, 208 E. Wisconsin Ave., Milwaukee 2, Secretary.

AMERICAN ACADEMY OF FORENSIC SCIENCES, Drake Hotel, Chicago, March 1-3. Prof. Ralph F. Turner, Michigan State College Dept. of Police Administration, East Lansing, Mich., Secretary.

AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS, Palmer House, Chicago, Jan. 27-Feb. 1. Dr. Harold B. Boyd, 122 S. Michigan Ave., Chicago 3, Secretary.

AMERICAN SOCIETY FOR SURGERY OF THE HAND, Palmer House, Chicago, Jan. 26. Dr. Joseph H. Boyes, 1401 S. Hope St., Los Angeles 15, Secretary.

ATLANTA GRADUATE MEDICAL ASSEMBLY, Municipal Auditorium, Atlanta, Ga., Feb. 5-7. Mrs. Stewart R. Roberts, 768 Juniper St. N.E., Atlanta, Executive Secretary.

CENTRAL SURGICAL ASSOCIATION, Chicago, Feb. 22-24. Dr. James T. Priestley, Mayo Clinic, Rochester, Minn., Secretary.

CHICAGO MEDICAL SOCIETY ANNUAL CLINICAL CONFERENCE, Palmer House, Chicago, March 6-9. Dr. Walter C. Bornemeier, 30 N. Michigan Blvd., Chicago 2, Secretary.

INTERNATIONAL POST-GRADUATE MEDICAL ASSEMBLY OF SOUTHWEST TEXAS, Municipal Auditorium, San Antonio, Jan. 23-25. Dr. John J. Hinchey, P. O. Box 2445, San Antonio 6, Secretary.

MIDDLE ATLANTIC STATES REGIONAL CONFERENCE, Philadelphia, Jan. 18. Dr. William Bates, 2029 Pine St., Philadelphia 3, Secretary.

NATIONAL CONFERENCE ON MEDICAL SERVICE, Palmer House, Chicago, Feb. 11. Dr. R. E. Fitzgerald, 2218 N. Third St., Milwaukee 12, Secretary.

NEW ORLEANS GRADUATE MEDICAL ASSEMBLY, Municipal Auditorium, New Orleans, March 5-8. Dr. W. D. Beacham, 1430 Tulane Ave., New Orleans 12, Secretary.

SECTIONAL MEETING, AMERICAN COLLEGE OF SURGEONS, Hotel Statler, St. Louis, Jan. 22-23. Dr. James Barrett Brown, 508 N. Grand Blvd., St. Louis, Chairman.

SOUTH CENTRAL BRANCH, AMERICAN UROLOGICAL ASSOCIATION, Hotel Adolphus, Dallas, Jan. 29-Feb. 2. Dr. Rex E. Van Duzen, 721 Medical Arts Bldg., Dallas, Chairman.

SOUTHEASTERN SECTION, AMERICAN UROLOGICAL ASSOCIATION, Peabody Hotel, Memphis, Tenn., March 7-10. Dr. Russell B. Carson, Sweet Bldg., Fort Lauderdale, Fla., Secretary.

DEATHS

Danahy, John Charles ⊕ Cincinnati; born in Cincinnati Sept. 1, 1900; University of Cincinnati College of Medicine, 1925; instructor in pediatrics at his alma mater; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; served in the U. S. Naval Reserve during World War II and was cited for service aboard a vessel in action in the South Pacific; director, department of health and hygiene, city board of education; on the staffs of Children's Hospital, Good Samaritan Hospital, St. Joseph Maternity Hospital and Infant Home and St. Mary's Hospital; died in Holmes Hospital November 7, aged 50, of myocardial infarction.

Brown, Albert Wheatland, Upper Darby, Pa.; born in Philadelphia Aug. 25, 1904; Jefferson Medical College of Philadelphia, 1931; formerly on the faculty of his alma mater; specialist certified by the American Board of Obstetrics and Gynecology; fellow of the American College of Surgeons; during World War II served overseas as a major in the Third Auxiliary Surgical Group in Africa, Sicily, Italy and the Normandy invasion; awarded the Bronze Star, Distinguished Unit Badge and seven campaign stars; served on the staff of Philadelphia Lying-in Hospital; chief of obstetrics and gynecology at the Fitzgerald-Mercy Hospital, where he died November 28, aged 46.

Munroe, Henry Stokes Jr., ⊕ Charlotte, N. C.; born in Columbus, Ga., Aug. 27, 1909; Duke University School of Medicine, Durham, 1935; certified by the National Board of Medical Examiners; fellow of the American College of Surgeons; specialist certified by the American Board of Surgery; served overseas during World War II; on the staffs of the Presbyterian, Mercy and Good Samaritan hospitals; consulting surgeon, Charlotte Memorial Hospital; died in the University of Pennsylvania Hospital, Philadelphia, October 29, aged 41, of pulmonary embolus.

Beavers, George H., Benjamin, Texas; Missouri Medical College, St. Louis, 1890; died in Fort Worth October 24, aged 84.

Brown, Frederick William ⊕ Watervliet, Mich.; Saginaw (Mich.) Valley Medical College, 1899; served as president of the village of Watervliet and as mayor; director and vice president of the First National Bank; on the staff of Mercy Hospital in Benton Harbor and Community Hospital; died in the Edward W. Sparrow Hospital, Lansing, November 18, aged 75.

Carpenter, Forest LaFon ⊕ Latta, S. C.; Vanderbilt University School of Medicine, Nashville, Tenn., 1904; past president of the Dillon County Medical Association; died in the McLeod Infirmary, Florence, November 22, aged 71, of coronary thrombosis.

Carr, Hilton Rice, Jackson, Miss.; Memphis (Tenn.) Hospital Medical College, 1909; served in France during World War I; formerly superintendent of the Shelby County Hospital; member of the rating board of the Veterans Administration Office; died in Baptist Hospital, Memphis, Tenn., November 17, aged 63, of chronic pyelonephritis.

Clover, Samuel Williams, Abington, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1898; formerly on the staff of the Women's Homeopathic Hospital in Philadelphia; died October 29, aged 76, of carcinoma of the liver.

Coe, Arthur Hamilton, Los Angeles; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1888; died October 26, aged 83.

Collins, Isaac Sidwell, Spokane, Wash.; Marion-Sims College of Medicine, St. Louis, 1897; formerly coroner and deputy coroner; died in Edgecliff Sanatorium November 2, aged 78, of arteriosclerosis.

Conley, James George ⊕ Pittsburg, Kan.; Marquette University School of Medicine, Milwaukee, 1915; served during World War I; died October 28, aged 63.

Cook, Mary, Montclair, N. J.; Woman's Medical College of Baltimore, 1903; died October 31, aged 85, of cardiovascular renal disease.

Copeland, Thomas Alexander, Holly Grove, Ark. (licensed in Arkansas in 1903); died October 23, aged 81.

Day, Edward, Maplesville, Ala.; Medical Department of Tulane University of Louisiana, New Orleans, 1911; member of the American Medical Association; died October 12, aged 66, of coronary occlusion.

Deuel, Avery George, Rock Springs, Wyo.; Nebraska College of Medicine, Lincoln, 1907; Queen's University Faculty of Medicine, Kingston, Canada, 1912; died November 12, aged 75, of cardiorenal disease.

Devlin, Hugh Joseph ⊕ Newark, N. J.; Baltimore Medical College, 1905; died October 24, aged 77.

Donald, Robert Lavalle ⊕ Meridian, Miss.; Jefferson Medical College of Philadelphia, 1930; served during World War II; affiliated with the Anderson Infirmary, where he died November 2, aged 46, of coronary thrombosis.

Esposito, Albert Americo, Brooklyn; Creighton University School of Medicine, Omaha, 1940; served during World War II; retired August 1, 1948 as a senior assistant surgeon in the U. S. Public Health Service reserve; died October 28, aged 39.

Farrell, Newton Henry ⊕ American Falls, Idaho; Creighton University School of Medicine, Omaha, 1913; mayor of American Falls; affiliated with Schlitz Memorial Hospital, where he died October 30, aged 62, of hypertension and cardiorenal disease.

Fletcher, Frank C., Gaysville, Vt.; University of Vermont College of Medicine, Burlington, 1893; died November 1, aged 81, of cerebral accident.

Flippin, Peter John, Kerrville, Tenn.; Memphis Hospital Medical College, 1897; died in the Baptist Hospital, Memphis, November 7, aged 77, of coronary thrombosis.

Fordyce, DeLorme T., ⊕ Conshohocken, Pa.; Temple University School of Medicine, Philadelphia, 1911; served on the staff of Wills Hospital, Philadelphia and Bryn Mawr (Pa.) Hospital; formerly a dentist; died November 6, aged 69, of arteriosclerotic cardiovascular disease.

Francis, William D., Lampasas, Texas; Missouri Medical College, St. Louis, 1897; for many years local physician and surgeon for the Southern Pacific lines; served as mayor of Lampasas and as city and county health officer; died in Austin recently, aged 92.

Gallaway, George Ellis ⊕ Rahway, N. J.; New York University Medical College, New York, 1898; served during World War I; formerly member of the city council; member and past president of the medical staff of Rahway Memorial Hospital; died in Lee Memorial Hospital, Fort Myers, Fla., November 19, aged 74.

Gerlach, Ella M., Philadelphia; Woman's Medical College of Pennsylvania, Philadelphia, 1898; for many years on the staff of Woman's Hospital; died October 5, aged 84.

Goodrich, Charles F., Washington, Mo.; Washington University School of Medicine, St. Louis, 1898; member of the American Medical Association; died in the Katie Jane Memorial Home in Warrenton, October 10, aged 75, of hypostatic pneumonia and myocarditis.

⊕ Indicates Fellow of the American Medical Association.

Gordon, Noel Eugene, Minonk, Ill.; University of Illinois College of Medicine, Chicago, 1930; member of the American Medical Association; affiliated with the Mennonite Hospital and St. Joseph's Hospital in Bloomington, where he died November 4, aged 47, of cirrhosis of the liver.

Kehres, Louis Jacob, Hudson, Ohio; University of Wooster Medical Department, Cleveland, 1895; died October 29, aged 88.

Kellam, Seth White, Dallas, Texas; Baylor University College of Medicine, Dallas, 1936; for a year served with the U. S. Public Health Service and in the medical corps of the U. S. Army during World War II; recently retired as medical director of Chance Vought Aircraft Company; died in Methodist Hospital, recently, aged 44, of rheumatic heart disease.

Kimberlin, Lester Olin ⊕ San Francisco; Cooper Medical College, San Francisco, 1911; died November 2, aged 66.

Lebeau, Samuel Israel ⊕ Pittsburgh; University of Pittsburgh School of Medicine, 1911; member of the American Academy of Pediatrics; died October 11, aged 65.

Lees, Robert Bruce, Los Angeles; University of Minnesota College of Medicine and Surgery, Minneapolis, 1901; died in Inglewood recently, aged 75, of heart disease and arteriosclerosis.

Levins, Nathan Noah ⊕ Boston; Tufts College Medical School, Boston, 1904; an Associate Fellow of the American Medical Association; on the staff of Beth Israel Hospital; died November 4, aged 76, of cerebral arteriosclerosis.

Lindsay, John Fergus, Youngstown, Ohio; Western Reserve University Medical Department, Cleveland, 1902; on the staff of Youngstown Hospital; died October 11, aged 72, of coronary disease.

Loomis, Francis William, Shannon City, Iowa; Barnes Medical College, St. Louis, 1894; died October 2, aged 93, of heart disease.

Lyon, William Tracy, Naples, N. Y.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1911; formerly a medical missionary; county coroner; served as health officer of the village of Naples and the towns of Italy and South Bristol; member of the school board; on the staff of the Wayland (N. Y.) Hospital; died November 1, aged 67, of coronary thrombosis.

McCartney, Harold Samuel ⊕ Mineola, N. Y.; Queen's University Faculty of Medicine, Kingston, Canada, 1927; on the staffs of the Meadowbrook Hospital, Hempstead, and the Nassau Hospital; county police surgeon for the third district; died November 9, aged 51.

McClure, James Hunter, Chicago; Meharry Medical College, Nashville, Tenn., 1916; died October 31, aged 65, of hypertension, nephritis and auricular fibrillation.

McCormack, Christopher Joseph ⊕ Hartford, Conn.; Yale University School of Medicine, New Haven, 1929; specialist certified by the American Board of Surgery; formerly fellow in surgery at the Mayo Foundation in Rochester, Minn., member of the Alumni Association of the Mayo Foundation, Alpha Sigma Phi, Phi Chi and Sigma Xi; consulting surgeon, Litchfield County Hospital, Winsted, and St. Francis Hospital, where he died October 6, aged 46, of coronary thrombosis.

Miller, Lawrence Robling ⊕ Winslow, Ind.; Kentucky School of Medicine, Louisville, 1907; served as secretary-treasurer of the Pike County Medical Society; died in the Welborn Memorial Baptist Hospital in Evansville November 3, aged 69, of cerebral hemorrhage.

Nichols, Asbury S., Sylva, N. C.; Tennessee Medical College, Knoxville, 1905; member of the American Medical Association; during World War II examining physician for Selective Service System in Jackson County; died November 6, aged 69.

Orsborn, George Earl ⊕ Denver; Denver College of Physicians and Surgeons, 1908; University of Colorado School of Medicine, Denver, 1912; died October 5, aged 70.

Pedrick, Franklin Burche, Washington, D. C.; New York Homeopathic Medical College and Flower Hospital, New York, 1913; member of the American Medical Association; died in Oteen, N. C., November 7, aged 64, of pulmonary tuberculosis.

Polanco, Mario ⊕ Upper Darby, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1928; specialist certified by the American Board of Internal Medicine; on the staffs of Fitzgerald-Mercy Hospital, Darby, and the Jewish Hospital, Philadelphia; died November 6, aged 48.

Polson, James Alexander, Bronxville, N. Y.; Queen's University Faculty of Medicine, Kingston, Ont., Canada, 1910; served on the staffs of the Seton and Bellevue hospitals in New York; trustee at his alma mater; died November 3, aged 65, of carcinoma.

Poston, William Henry ⊕ Pamplico, S. C.; Medical College of the State of South Carolina, Charleston, 1909; died November 6, aged 69.

Recker, Wayland Bernard ⊕ Leipsic, Ohio; St. Louis University School of Medicine, 1926; member of the American Association of Railway Surgeons; past president of Putnam County Medical Association and the Northwestern Ohio Medical Society; on the staffs of the Memorial and St. Rita's hospitals in Lima and the Findlay (Ohio) Hospital; died October 29, aged 48, of heart disease.

Regier, Wilhelm Edward, White Water, Kan.; University Medical College of Kansas City, 1907; member of the American Medical Association; on the courtesy staff of Bethel Deaconess Hospital in Newton; died October 24, aged 67, of coronary thrombosis.

Schmidt, Harry Burke, Detroit; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1911; formerly associate professor of clinical medicine at the Wayne University College of Medicine; formerly on the staff of Providence Hospital; died November 4, aged 68, of acute pulmonary edema.

Shedd, John Z., North Conway, N. H.; Medical School of Maine, Portland, 1891; member of the American Medical Association and in 1910, 1912 and 1913 a member of its House of Delegates; served as health officer; died October 16, aged 89.

Slocumb, Clyde Buchanan, Doerun, Ga.; Atlanta School of Medicine, 1912; member of the American Medical Association; died October 29, aged 63.

Stetner, Walter Lewis, Milwaukee; Northwestern University Medical School, Chicago, 1938; served during World War II; died in Wauwatosa October 11, aged 44.

Stevenson, Frank Burton, Indiana, Pa.; Jefferson Medical College of Philadelphia, 1908; member of the American Medical Association; affiliated with Indiana Hospital; died in the Veterans Administration Hospital, Aspinwall, October 31, aged 68, of brain tumor.

Vaughan, Roger Throop, Chicago; Rush Medical College, Chicago, 1903; clinical associate professor of surgery, emeritus (Rush) University of Illinois College of Medicine; professor of surgery at the Cook County Graduate School of Medicine; served during World War I; member of the Western Surgical Association; fellow of the American College of Surgeons; assistant warden at Cook County Hospital, where he died November 13, aged 72, of coronary disease.

Vonden Steinen, Edward, Tucson, Ariz.; Western Reserve University Medical Department, Cleveland, 1905; member of the American Medical Association; honorary member of the Colorado State Medical Society; formerly director of athletics and professor of physical education at his alma mater and director of student health and professor of physical education at Colorado State Teachers College, Greeley; served during World War I; died October 10, aged 74, of cerebral hemorrhage.

FOREIGN LETTERS

NORWAY Oslo.

Medical Department A of the Rikshospital.—Despite its many wards, large and small, all on the same floor in the Rikshospital in Oslo, Medical Department A has an esprit, an atmosphere, all its own. One senses it, consciously or unconsciously, whether one is a doctor, a nurse or a patient. An address by Prof. Olav Hanssen on the occasion of his retirement from the directorship of Medical Department A was published in *Tidsskrift for Den Norske Laegeforening* for Nov. 1, 1950. For 25 years he has been responsible for the esprit of the department, and now he shows how he worked to cultivate it. In his opinion the ideal physician must have patience, tact, tolerance, loyalty and respect for the patient's secrets. On the subject of the good listener he refers to Gerhard Gran's analysis of his compatriot, Moltke Moe, who "listened out of us our half-thoughts, notions and feelings of which we had hitherto been unconscious. Looking back on our conversations I remember not so much the things he said as the things he induced me in some queer way or other to say myself."

Another event likely to make one think about the esprit of a hospital happened last fall, when the matron of Medical Department A, Miss Lina Andersen, was awarded the King's gold medal in token of her services to nursing. The ceremony on this occasion was informal and unpretentious, in the spirit of a nurse who has practiced self effacement all her life. Many years ago Sister Lina abandoned a promising career as a journalist to take up nursing. Her team of nurses is recruited mainly from a religious (Lutheran) body, Diakonissehuset, which for more than 80 years has conducted a school of nursing. Speaking of her in his address, Professor Hanssen said, "If the patients in Medical Department A have sometimes felt that they had not lost their identity, but were living as it were at home, it is the department's matron to whom the credit belongs in a marked degree."

There is yet another feature of the esprit of Medical Department A—a spirit of adventure and exploration fostered by Professor Hanssen's successor, Prof. Paul Owren, who came to his task with an international reputation for his work on blood clotting. All his colleagues in Norway know something about this work, and now, when they are in doubt about some obscure disease of the blood, they refer the case to Medical Department A.

May Quacks Be Paid out of Public Funds?—At present the national sickness insurance funds can be drawn on only by duly qualified medical practitioners, not by any other group of healers, however pleased their patients may be with them. On Nov. 1, 1950, at a meeting of the Norwegian Parliament, one of its members, Herr Lavik, pleaded for a change in this respect. He said he held statements from more than 400 persons who had been cured by nature healers and homeopaths. In his opinion the results of treatment are a better guide to its efficacy than any legal qualification to practice medicine, and the quack who is clever enough to discover the cause of a disease cannot in all fairness be accused of practicing quackery. After he had referred to several cases in which nature healers had cured patients abandoned by doctors, he was informed by another member of Parliament that one of the patients he had mentioned, cited in Parliament last June as cured, had died of cancer in October. Herr Lavik's championing of the nature healer on this occasion failed to draw from the government any pledge of indemnification out of public funds.

A reference during the same debate to the possibility that the antiquackery law of 1936 may soon be revised indicates that the law leaves broad scope to unqualified medical practitioners. To be sure, it reserves only to duly qualified medical practitioners the treatment of epidemic diseases, tuberculosis, venereal disease, cancer, diabetes, dangerous anemias and goiters with morbid manifestations, but the ailments coming under none of these headings are so numerous that the field left open to faith healers, nature healers and all the other healers with suggestively attractive titles is very wide—so wide, in fact, that there is an uneasy feeling in the quack world that any revision undertaken with regard to this law may mean a process of tightening up rather than of slackening.

Treatment of "Seal Finger" with Aureomycin.—In the town of Tromsö in Northern Norway, Dr. Per Waage has recently studied 34 sealing and allied expeditions on their arrival in this port, and he has found 30 of the members of their crews to be suffering from "seal finger." It is supposed to be an infection from seals and is characterized by the glistening appearance of the swollen and painful finger. Under expectant treatment it tends to last five to six months or more. Twenty of these patients were treated with aureomycin. The results were very satisfactory, and after only three or four doses there was considerable relief of pain; after two days the swelling was much reduced and the finger less tense. When the joints were not involved, the patients could be discharged as cured after a week or two. In view of the clinical similarity of "seal finger" to erysipeloid, Dr. Waage suggests that this disease also may prove amenable to aureomycin therapy.

SWEDEN

International Course on Audiology in Stockholm.—The first international conference on audiology was held in Stockholm in 1948 on the initiative of Prof. Gunnar Holmgren, editor of *Nordisk Medicine* and *Acta Oto-Laryngologica.* Encouraged by the response to it, he organized a special international course on this subject in Stockholm Sept. 10-20, 1950. He secured the attendance of some two score lecturers, including 10 from the United States. Altogether 260 delegates from a score of different countries attended this course, which was held in Commercial High School in Stockholm. The course was so arranged that 12 lectures were given every day in four different rooms.

On the opening day and in the presence of a representative of the royal house and delegates from the government and other official bodies, Professor Holmgren traced the development of audiology as a comparatively new discipline, worthy of attention as an important specialty. He also gave an account of the plans for a Central Hearing Institute to be created in Sweden under the auspices of the Royal Committee for Combating Deafness. The subsequent addresses and lectures were organized under several different headings, one of which was concerned with the anatomy, physics, physiology and psychology of hearing. Another main section of the course was devoted to the surgery of otosclerosis. Other subjects were deafness in childhood and special methods of examination.

Before and after attending one or other of these lectures, the participants in this course formed themselves into small groups of 10 to 20 under the guidance of the lecturers in order to discuss earlier lectures and to acquire dexterity in methods of examination and treatment. Films, most of which were on loan from Societas Medica Scandinavica, were shown daily. Between lectures the visitors made study excursions to centers of interest, such as the new acoustic laboratory of Technical High School, the ear departments of various hospitals and a school for the deaf and dumb. The course was also supplemented by an exhibition of instruments, hearing aids and devices for the measurement of hearing. A report will shortly be published of the lectures and demonstrations given during this course in a supplement to *Acta Oto-Laryngologica.*

The items in these letters are contributed by regular correspondents in the various foreign countries.

Death of Dr. Gosta Forssell.—The grand old man of Swedish radiology, Dr. Gösta Forssell, professor emeritus of radiology at the Caroline Institute, died of heart failure on November 13. Forssell was born in 1876 in Dalecarlia. As a medical student he began to study radiology, and in 1906 he established in the Serafimer Hospital (Serafimerlasarettet) in Stockholm the small x-ray laboratory that developed under his hands into a renowned institution. He was the head of this institution from 1906 to 1941. In 1910 he started the little hospital Radiumhemmet with 16 beds, one x-ray machine and 120 mg. of radium. It became one of the best radiotherapeutic centers in the world. It is now the King Gustaf V Jubilee Clinic at the Caroline Hospital (Karolinska Sjukhuset). Forssell was one of the founders of this hospital. In 1917 Forssell was appointed the first professor of medical radiology at the Caroline Institute. He left this chair in 1941.

Forssell has written about 200 scientific papers. He was particularly interested in the autoplastic muscular movements of the gastric mucosa; and he continued work in this field after retirement. He was the founder of *Acta Radiologica* and was editor of this periodical until his death.

Forssell was a brilliant organizer. To him belongs much of the credit for the advance of radiology in Sweden. When he retired, in 1941, he left to his successors five well equipped institutions in Stockholm for radiologic research. He had great skill in persuading the parliament to vote money for radiotherapy; he was a master in raising funds for such purposes and for scientific research.

Forssell participated, in 1925, in the first international radiologic congress, in London, and it was under his leadership that the second world congress on radiology was held in Stockholm in 1928. He was honorary member in most radiologic societies in the world. In the summer of 1950 he was a member of the Royal Society of Medicine in London. At the great festival in the Stadion of Stockholm in 1947 to celebrate King Gustaf's eightieth birthday, Forssell spoke to the king on behalf of the Swedish people.

Personally charming and kind, Forssell was beloved by the medical students in Stockholm, whose honorary chairman he was for many years. He was beloved also by his many pupils and by his patients from all parts of Sweden.

DENMARK COPENHAGEN.

Dr. R. K. Rasmussen and Psittacosis in the Faroes.—On Oct. 2, 1950, the University of Copenhagen conferred the degree of Doctor of Medicine *Honoris Causa* on Dr. Rasmus Kristen Rasmussen, a general practitioner who has spent most of his long professional life under strictly rural conditions in the Faroes, a dependency of Denmark. When he left a promising career at home to work in the wilds, his friends thought he was wasting his talents, but he soon sent epidemiologic studies to Denmark for publication. His reports dealt with acute epidemic myalgia, the epidemiology of tuberculosis and certain aspects of whooping cough. As early as 1925 he showed that congenital immunity to whooping cough must be rare and that reinfection with it is common.

Rasmussen's most important discovery, perhaps, was his identification of epidemic alveolar pneumonia (described as such by his compatriot Dr. A. A. Vaag) with psittacosis. Studying Vaag's account of an epidemic of pneumonia in the Faroes, Rasmussen observed its similarity to psittacosis. He suspected that the source of infection might be the fledglings of the gull Fulmaris glacialis, counted as a delicacy in the Faroes. He communicated with authorities on the subject in Copenhagen, London and Berlin, and dead fledgings, blood from patients suffering from alveolar pneumonia and tissues from patients dying of this disease were sent to Copenhagen. Thence they were sent by air to London and Berlin. In London, Professor Bedson performed complement fixation tests with the serum of three patients, and in Berlin Haagen and Mauer showed that mice reacted to Rasmussen's specimens in the same way as to the virus of psittacosis. The virus of psittacosis was also cultivated from the blood and other tissues of a woman dying of alveolar pneumonia. This happened in 1938, and, had it not been for World War II, Rasmussen's discovery would long ago have become well known. It is a masterpiece of detective work by an "ordinary" general practitioner out of direct touch with any laboratory but endowed with a speculative, analytic mind and with time most usefully spent in keeping up to date in his reading and correlating the clinical findings of others with the knowledge of laboratory workers.

Coordination of General Practitioners with Specialists and Hospital Doctors.—At a meeting on Aug. 27, 1950, leading members of the Danish Medical Association discussed in detail the ways and means by which better teamwork could be organized between general practitioners, specialists and hospital doctors. It was pointed out that a committee has recently been appointed to investigate sickness in the community and how to deal with it by the aid of general practitioners and hospital services. Of the sum of 300,000 kroner put at the hospital of this committee, half has been provided by the Rockefeller Foundation, the other half by private institutions. In the near future Copenhagen will be spending more than 100,000,000 kroner on hospital services and the whole of the country two or three times this sum. So it behooves all concerned to see that these sums are not spent till the relations between general practitioner and hospital are defined in the best interests of the community.

There was one concrete suggestion made at this meeting that offered a useful bridge between general practitioner and hospital. It was to the effect that general practitioners should spend their holidays as substitutes for hospital interns and that the latter should take on holiday duties for general practitioners. This suggestion was first made, by the same person, 30 years ago at a medical meeting.

MEXICO

Ninth National Assembly of Surgeons.—From November 19 to 25, Mexico City was host to leading surgeons from all over the country, Central and South American, and the United States. The occasion was the ninth National Assembly of Surgeons. These meetings take place in Mexico City every two years, during the last week of the month of November, at the Hospital Juárez, one of the oldest in Mexico and known till the last part of the nineteenth century as Hospital de San Pablo. This institution is the city hospital.

The assembly includes official addresses, reports of the 20 sections and surgical demonstrations. The convention also included specialty meetings, such as the first Mexican meeting of orthopedic surgeons, the third national meeting of anesthesiologists and the seventh national convention of nurses. There were 13 official addresses and more than 350 papers read at the section, many of them part of symposiums.

Among the official addresses that caused much commentary may be mentioned that of Mario Valles and co-workers, who presented the experiences of the Mexican Red Cross on thoracoabdominal wounds. Dr. Clemente Robles, representing the National Academy of Medicine, discussed the ethical aspects of surgical practice. In his paper the speaker emphasized the necessity of more careful selection of medical students and also the need of closer relation between surgeons. Dr. Bernardo Sepúlveda and Dr. Manuel Quijano, from the Hospital de Enfermedades de la Nutrición, stressed the importance of liver biopsy and liver function tests in the surgical management of patients with liver disease. Dr. José Ramírez Gama summarized the present status of pulmonary resection in the treatment of pulmonary tuberculosis, according to their observations in the Gea González tuberculosis hospital. Dr. Aguirre and collaborators, from the Hospital Juárez, discussed treatment of traumatic ruptures of the urethra.

Dr. Otero read a paper on new technics of cesarean section. In the symposium on sterility, Dr. Alvarez Bravo spoke on the role of noninfectious diseases of the ovarian tubes. Dr. Weinstein (New Orleans) discussed results he had obtained with ligature of the inferior cava in puerperal phlebitis. Dr. Ayala González (Hospital General, Mexico City) spoke on the postcholecystectomy syndrome. In the radiology section the paper of Dr. Deschamps, from the Hospital de Enfermedades

de la Nutrición, was of considerable interest; the author demonstrated the diagnostic utility of injection of oxygen in the retroperitoneal space, to permit visualization of tumors in that site. The section on plastic surgery had the largest number of foreign contributions. This section had interesting round tables.

The assembly was a complete success, from both the scientific and social points of view. It may be considered as an index of the progress made by Mexican surgery during the last years.

COLOMBIA BOGOTÁ.

Toxoplasmosis.—Drs. Manuel Roca-Garciá, Jorge Camacho-Gamba and Gonzalo Esguerra-Gómez reported the first case of human toxoplasmosis in Colombia at the National Academy of Medicine on October 19. Toxoplasma had been found in guinea pigs in Colombia in 1944 by Drs. Luis Patiño-Camargo, Julián De Zulueta and Gabriel Toro-Mejía and the organisms noted in dogs and marsupials by other investigators.

The patient was a 40 day old infant, born in Bogotá. The main symptoms were jaundice, hepatomegalia, splenomegaly, hydrocephalus and eosinophilia. Roentgen examination disclosed signs of periostitis of both femoral diaphyses and on the posterior middle region of the right tibia and numerous, small, intracranial calcifications. (The authors do not believe that the differential diagnosis of toxoplasmosis and torulosis as proposed by Neuhauser and Tucker could be based on the size of the spleen, which, in torulosis is very large; in their case splenomegaly was much more pronounced than hepatomegalia.) The blood contained 6.6 mg. of bilirubin per 100 cc., and the direct van den Bergh reaction was highly positive. The cerebrospinal fluid showed a decided increase in albumin, lymphocytes and xanthochromia. Colloidal benzoin precipitated in the first five and the last five tubes. The result of the test of the patency of the aquaeductus cerebri was negative. The intradermal reaction with toxoplasmin was positive in the mother and negative in the infant. Complement fixation and in vitro neutralization tests yielded positive results for both mother and infant. The mother showed no sign of illness either during pregnancy or after the birth of her child. Treatment consisted of the administration of penicillin, arsenic, sulfadiazine and aureomycin. The patient was observed until she was 10 months old, at which time jaundice had disappeared, the liver and spleen had diminished in size, hydrocephalus had increased and there were symptoms of increased intracranial pressure and arrest of growth and mental development. Toxoplasma was isolated from the centrifuged cerebrospinal fluid and was injected into white mice. Fifty serial passages by intracerebral inoculation and 48 passages by intraperitoneal inoculation were made. None of the infected mice survived, and the virulence of the parasitic organism increased to 1:100,000 on the fiftieth passage. The organism was virulent for guinea pigs, rabbits and small chickens. The protozoan is approximately 4 to 6 microns long and 2 to 3 microns wide. Generally, it is long and slightly curved, and frequently one end of its body is less rounded than the other. The nucleus is clear and almost always located toward the more rounded portion. Multiplication occurs through longitudinal division. It has been identified as Toxoplasma gondi. The studies on which this report was based were made at the Carlos Finlay Institute of Special Studies, which is cooperatively maintained by the Ministry of Hygiene of Colombia and the Pan American Sanitary Bureau.

Biologic Conditions in the Plateaus of Bogotá.—Prof. J. Hernando Ordóñez, in a study published in the *Anales de la Sociedad de biología de Bogotá* (July 2, 1950), reviewed the literature concerning the biologic adaptations of people living in the plateaus of Bogotá at 2,460 meters above sea level. He included his own observations on arterial blood pressure, normal electrocardiograms and melanosis of unknown origin. The author's conclusions are as follows: 1. The oxygenation of the blood is normal or almost normal in persons living in Bogotá. 2. At this altitude the pulse is normal, the arterial blood pressure is not modified and the electrocardiogram does not show any sign of anoxemia. 3. No modifications of the metabolism, respiration or the nervous system were observed. Some slight symptoms of chronic altitude sickness were observed. 4. Diffuse melanosis, due to the lack of some nutritional factors, was observed. It seems that altitude may play a secondary role in the pathogenesis of melanosis. 5. Further studies, e. g., on heart and lung diseases and on physical exercise, are needed.

Social Welfare.—The Colombian Institute of Social Welfare celebrated its first anniversary on September 26. At first there were 70,000 insured persons in Bogotá. Now there are 100,000 in Bogotá and 60,000 in Medellin. In the near future benefits will be extended to the Quindío region. The following services are included: 1. Medical care, hospitalization, drugs, surgical treatment, laboratory services and roentgen examinations. Benefits are for a maximum period of 26 weeks from the first day of illness. 2. If an illness incapacitates the insured for work, a cash subsidy for a maximum period of 180 days is granted. 3. Periods of rest for prevention of diseases and convalescence. 4. Dental care. 5. Periodic medical examinations. 6. In case of pregnancy, the insured will receive for an eight week period a daily subsidy equivalent to her daily total salary and complete medical care before and after delivery. 7. Obstetric care is given the wife of the insured worker. The following figures were issued by the Institute of Social Welfare for the period Sept. 26, 1949 to Aug. 31, 1950: 140,593 medical consultations, 12,777 medical visits to the home, 3,819 surgical interventions, 3,760 deliveries, 10,133 hospitalized persons, 7,615 roentgen examinations, 160,346 laboratory examinations, 176,351 prescriptions filled, 305,323 vaccinations, 105,787 dental consultations and 36,216 dental extractions.

Professor Uribe Uribe Honored.—The Colombian Society of Internal Medicine celebrated its first anniversary on October 27 with a banquet at the Medical Club of Bogotá in honor of Prof. Alfonso Uribe Uribe, the president of the society. All the physicians of Bogotá and the members of all the scientific societies joined to pay homage to the man, who is professor of clinical medicine at the National University and has devoted his life to the progress of medicine. On this occasion Professor Uribe Uribe said: "We, as doctors, should be very interested in a technical and specialized pragmatism which favors a simple and perfect goal. Also, we should be concerned with the researchers with panoramic vision and vast horizons since they are the ones who are progressively determining, with the aid of experimental medicine, more exact knowledge on pathology, physiology and the treatment of diseases. The successful structure of a medical art that strives to preserve health and to cure disease is dependent on these advancements. It is an art to talk to a patient and, with friendship, perceiving his preoccupation, anguish and fear, to experience, sympathetically, these feelings with him. It is an art to gather together the facts of the evolution of a disease and to analyze them correctly; to look, aided by irreproachable mastery, for symptoms that are evident to the senses and those that can be supplied by scientific technics as applied to medicine; to integrate the diagnosis, prognosis and treatment of a disease into an exact synthesis that will alleviate the patient's pain and ease the mental disquietude of the patient and of those around him. Finally, it is an art not to do harm at any time either to the body or the mind of the patient and not to cause his relatives distress. Thus have I understood and practiced medicine, as a doctor at the patient's bedside, in a bedroom filled with the anguish of possible death or in a consultation room full of hope for health and life. Thus have I demonstrated my devotion to medicine to those who wanted to be at my side. I value the title that you have wanted to give me, namely, the title of teacher. However, it seems to me that I do not merit the title simply because I may have contributed something to science or to technical advancements. I think that, perhaps, the enthusiasm, good will and sincerity that I have shown as a doctor, and the factors that contributed to my character as a doctor, justify my receiving the title. This is my doctrine. If it has been useful, I offer a toast, acknowledged by all of you, happy to see that the sick will be cured because the disciples work well."

CORRESPONDENCE

DIANETICS

To the Editor:—With considerable anxiety I have watched the cult "dianetics" develop from the first appearance of its principles in *Science Fiction Magazine*. I am concerned about its growth and popular acceptance, and I fear that the world has had dumped on it a new therapy which will have the staying power of chiropractic, with as little scientific background to support it.

It is a phenomenon of some sort, and full of meaning, that over 500,000 copies of the book are supposed to have been sold. Countless persons, without proper background and without understanding of basic human motives and drives, are "auditing" each other, and as a result mental hospitals may receive as patients many whose first psychotic breakdown occurred during such "auditing." The "auditors" simply do not know how to handle the material elicited. The dangers inherent in such amateurish "auditing" are readily apparent. Since these persons cannot recognize an incipient psychosis, adequate treatment may be delayed, and delay, as pointed out in Bellak's book, "Dementia Precox," definitely reduces the chances for recovery or improvement.

In a short time there has developed a demand on the part of thousands of persons for training as professional "auditors." To meet this demand, I am informed, there have been established two training centers in the United States, in Elizabeth, N. J., and in Los Angeles. The course lasts one month, and tuition is said to be $500. The initial Los Angeles enrolment was 1,000 persons, many having been turned away. An income of $500,000 for the Dianetic Foundation in one month is certainly not bad. This, however, is only the beginning. There is being projected a Dianetic College or University, with a two year course, which will no doubt give graduates greater prestige.

Devotees of dianetics, like the devotees of cults, are not moved by unfavorable statements made by men of recognized scientific background. These fanatics support the new cult with a religious fervor. In vain have I shown them comments by scientific critics. One gets the same answers that have so often been heard from enthusiasts for other cults. For one thing, one hears that the medical profession is really a medical trust that is trying to keep out all forms of treatment but its own. The new cult is growing by the vigorous exploitation of testimonials. I have already listened to a testimonial of a cure of agoraphobia. Another person has reported that since he has been "audited" he is a better conversationalist. One woman I know is about to start being "audited" after listening to a testimonial by someone who had gotten rid of many "engrams" through dianetics. This dianeticized person claimed that her thinking had improved and hence her abilities as a stock market trader had become markedly sharper, the whole process resulting in her taking profits of $13,000 within a few days. And so the testimonials go.

In Los Angeles the dianetics enthusiasts meet every Sunday morning in a theater to hear about the latest procedures and to listen to exegeses of the great book. As one would expect, the spirit of these meetings has the coloring that goes with religious zeal. At one of these meetings I saw one man get up and call attention to some contradictory phases of the teachings of the book. He was booed and hooted down, to the relief of the moderator. Professional "auditors" are setting up offices throughout the country and advertising for patients in the good old chiropractic way. Something should be done to expose irrefutably this nonsensical tomfoolery.

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SULFONES IN THE CHEMOTHERAPY OF LEPROSY

To the Editor:—Johansen and Erickson, in their article entitled "Current Status of Therapy in Leprosy" in THE JOURNAL (**144**:985 [Nov. 18] 1950), give adequate information by reference or otherwise as to the origin and source of the compounds they used, except 4-amino,4'-beta-hydroxyethylaminodiphenylsulfone (HES). This compound was synthesized, studied and tested for activity in experimental tuberculosis for the first time in the laboratories of the National Institutes of Health by my associates and me (Smith, M. I.; Jackson, E. L.; Junge, J. M., and Bhattacharya, B. K.: *Am. Rev. Tuberc.* **60**:62 [July] 1949; Smith, M. I.; Jackson, E. L., and Bauer, H.: *Ann. New York Acad. Sc.* **52**:704 [Dec.] 1949). The compound was generously supplied by Merck & Company, Inc., through Dr. Augustus Gibson, who offered to make it in sufficient quantity to be available for clinical tests in tuberculosis and leprosy. The work on tuberculosis has been in progress for nearly one year and a half at Freedmen's Hospital, Washington, D. C., by Dr. Howard M. Payne and his associates.

MAURICE I. SMITH, M.D.,
National Institutes of Health,
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LIVER PUNCTURE FOR DIAGNOSIS

To the Editor:—Ange Gabriel Maximé Vernois (1809-1877) in his thesis "Du diagnostic anatomique des maladies du foie, et de sa valeur au point de vue thérapeutique" (Paris, J. B. Baillière, 1844; Félix Malteste et Cie, 1844) discusses liver puncture biopsy for diagnostic purposes. Yet Vernois' early work is not mentioned in the many recent publications on liver puncture biopsy. Iversen and Roholm (1939), Luigi Lucatello (1895), W. E. King and his associates (*M. J. Australia* **1**:697 [June 5] 1948), G. Pascale, T. Grier Miller, Chester M. Jones, Bingel and Olivet, McMichael and Sherwood (England), Jones and Volwiler (Boston), Schiff (Cincinnati), Edwin Rasberry (University of Pennsylvania), Winston K. Shorey and the many other writers have failed to give credit to Vernois for his early ideas and observations. Julian Hoffman and Julius Rosenthal (*Ann. Int. Med.* **33**:1203 [Nov.] 1950) in their paper on liver biopsy, Buck (1949), Kumpe (1947), Hoffbauer (1947), and all other writers on the subject fail to mention Vernois' thesis.

HYMAN I. GOLDSTEIN,
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SOCIALIZED MEDICINE

To the Editor:—Much theoretical tripe has been written about socialized medicine. Since the proof of the pudding is in the eating, the real test is how the system operates in actual practice. For those near-sighted members of our profession who still insist that socialization of medicine will cure all our problems, both imaginary and real, the following excerpt from a letter just received from a fellow practitioner in England may be instructive.

"You are fortunate indeed I imagine, in America, in that you do not labour under nationalised medicine as we do. One's every activity is checked and rechecked by a horde of highly paid clerks who have arisen overnight and who delight in sitting on the doctor's back. It is very discouraging, as these are the people who earn the money, and being usually people of little education are pleased to wield their new authority on any matter, medical or otherwise.

"You will detect that I am a man with a grievance but I am still clinging to my interest in blood transfusion work. I do not suppose you know of any openings for Englishmen in blood transfusion in the United States? If you do I should be very interested to hear from you again."

A. S. WIENER, M.D., 64 Rutland Road, Brooklyn.

BUREAU OF INVESTIGATION

HADACOL—THE ETHICAL(?) PROPRIETARY

Hadacol is advertised as that "new, miracle-working medicine [which] brings wonderful new hope to sickly, ailing men and women." It is an elixir of 12 per cent alcohol, to which has been added some of the B complex vitamins, with iron, calcium, phosphorus, dilute hydrochloric acid and honey. It sells for $1.25 for a half-pint bottle.

According to the advertising trade magazines, its promotion has been so successful that its promoter, Senator Dudley J. LeBlanc of the Louisiana legislature, is hard put to find ways and means of spending the profits, and it seems that, no matter which way he turns, the resulting "unwanted" profits have been fabulous. It is widely advertised in newspapers and on billboards, with testimonials playing an important role in the promotion. It was even advertised in the family size as a Christmas present.

Hadacol now is also being promoted as an "ethical preparation" for use by physicians in their practice. In a form letter dated Nov. 6, 1950, bearing the facsimile signature of the "clinical research director," there is stated:

"Dear Doctor:

"In order that you may give consideration to HADACOL for its therapeutic effect in deficiencies of Vitamins B_1, B_2, Niacin and Iron . . . we suggest that you check and return the accompanying reply card, so that we may send you professional samples.

"It should be noted that HADACOL is also available under a PRESCRIPTION 'X' label. If you desire this special label on the professional samples sent you, please indicate your preference.

"As the accompanying reprint points out . . . HADACOL is recommended for a number of clinical deficiencies, and is especially indicated in febrile and debilitated cases, supplementing essential elements lost through restricted diets. HADACOL is effective in both pre- and post-operative cases, and is acceptable to old and to young alike.

"Optimum requirements of Vitamins B_1, B_2, Niacin and Iron are available in this well-balanced product . . . with beneficial amounts of Phosphorus and Calcium. The form is stable and palatable; the elements are readily assimilable.

"A clinical research program has been set up by us, which is now being put into effect. We cordially invite you to conduct clinical tests, among a group of your own patients, with HADACOL . . . on a fee basis per patient. It is suggested that you write us, at your convenience, if you are interested.

Fraternally yours,
THE LEBLANC CORPORATION
Leslie A. Willey, M.D.
Clinical Research Director"

The New Orleans *Item* for Sunday, Dec. 17, 1950, carried an eight-page supplement entitled "Amazing Story of Hadacol." Included in this supplement is a box headlined as follows: "DR. WILLEY, MEDICAL EXPERT, MAKES TESTS AND ANSWERS QUESTIONS." Therein it is also stated:

> "The makers of HADACOL make no move in improving their product, or in testing each unit of production, without the say-so of a medical expert. This expert is Dr. L. A. Willey.
>
> "Dr. Willey, who of course is a graduate of medicine and a licensed practitioner, is the medical director of the giant LeBlanc Corporation. From his clinic in Lafayette, Louisiana—the heart of the Evangeline country—Dr. Willey directs activities of 20 other medical experts throughout the country, who co-operate in clinical work for HADACOL.
>
> "Dr. Willey and his associates answer all questions concerning HADACOL that emanate from medical sources. The careful tests and scrupulously honest answers made by Dr. Willey and his clinical associates are some of the reasons why HADACOL is recommended by many doctors."

Some inquisitive physician-recipients of the form letter checked their 1950 American Medical Directory and were unable to find therein the name of the "clinical research director" of the LeBlanc Corporation. Although its biographic records are the most complete extant with respect to physicians, interns, medical students and graduates, and even cultists, the Directory Department reports it has no biographic record of the man.

The Bureau of Investigation does, however, have a record of Leslie A. Willey, but not as "M.D." In 1943 there was an inquiry about a "Dr." L. A. Willey of Newport Beach, Calif. The Directory Department asked the California State Board of Medical Examiners for information. According to the Board, Willey's name was not included in its license lists of doctors of medicine or cultists. The board's investigators apparently checked up on the matter, because in the annual report for 1944 it was stated that Leslie A. Willey had first pleaded not guilty to a charge of practicing without a license and unauthorized use of the term "doctor," then changed his plea to guilty to the charge of practicing without a license and was fined $250. Inquiry of a physician in Newport Beach, Calif., brought the observation that Mr. Willey was a male nurse who was conducting some sort of emergency hospital, but that he had been arrested and had left town.

It is hoped that no doctors of medicine will be uncritical enough to join in the promotion of Hadacol as an ethical preparation. It is difficult to imagine how one could do himself or his profession greater harm, from the standpoint of the abuse of the trust of a patient suffering from any condition. Hadacol is not specific medication. It is not even a specific preventive measure. It could not be eligible for serious consideration by the Council on Pharmacy and Chemistry. It smacks of the old "patent medicine" promotional efforts. In 1942 the Council announced that alcoholic elixirs of thiamine hydrochloride were not acceptable for "New and Nonofficial Remedies." In its report it stated:

> "It appears to the Council that preparations of this character are undoubtedly intended for repeated and prolonged administration. They will likewise be administered as a tonic to children. The Council feels that it is hardly in the interest of rational therapeutics to make it necessary to take appreciable amounts of alcohol in order to obtain a small amount of thiamine hydrochloride. In addition to this there is no good pharmacologic reason for the incorporation of thiamine hydrochloride in an alcohol solution, and therefore such preparations constitute an unscientific mixture of two therapeutic agents. Physicians who may wish to prescribe alcohol have ready access to this drug in various forms, including preparations listed in the U. S. Pharmacopeia and National Formulary. The Council felt that the use of a preparation of thiamine hydrochloride in an alcohol menstruum lends itself to abuse through over the counter sales" (*J. A. M. A.* **118:**980 [March 21] 1942).

Although Hadacol has been advertised to the laity as being a more assimilable form of administration for the vitamins, neither the U. S. Pharmacopeia nor the Council recognizes alcoholic elixirs containing these substances as a dosage form.

In some of its advertising the firm has offered to show that, while many other manufacturers might mix alcohol and vitamins, it remained for the Hadacol firm to use nothing but quality products in the composition of its preparation. For instance, it advertised in a Virginia newspaper in part as follows:

> "The continued increasing demand for HADACOL, one of the truly great medical discoveries given to the world by Senator Dudley J. LeBlanc [Could Senator LeBlanc have reference here to his early promotion of "Happy Day Headache Powders," an acetanilid preparation seized in 1940 by the government as being "dangerous to health when used according to directions?"—ED.] has made it necessary to decrease the ration allowance on HADACOL from six to two bottles.
>
> " 'We placed the limit at two bottles to a customer only after trying every other alternative,' said Senator LeBlanc in Lafayette, La. 'The demand for HADACOL has increased 1,000 per cent in the past year.
>
> " 'When I created HADACOL I read every available authoritative medical and drug book in order to use the very finest ingredients regardless of cost. I read on page 234, U. S. Dispensatory, 23rd edition [the twenty-fourth edition has been in print since 1947.—ED.] that "Theoretically Calcium Glycero-

phosphate should for many purposes be superior to most other calcium salts because it represents both calcium and phosphoric acid in a soluble combination." [Perhaps in his literary searches he should have read the "Epitome of the Pharmacopeia and National Formulary" (eighth edition, 1947). There he would have found under calcium glycerophosphate, N. F.: "Formerly used in neurasthenias, to improve the nutrition of the nervous system. There is no evidence that it has any value in such conditions."—ED.]

" 'Little did I realize when I made Calcium Glycerophosphate a part of the now famous HADACOL formula that in time the demand for this great medical discovery—HADACOL—would be so great that we would use up the entire available supply in the United States of this product.'

"Yes, in HADACOL, Senator LeBlanc envisioned the medicine that would bring blessings to folks of all ages. Perhaps others could have placed the same ingredients in a medicine, but it remained for him to develop a formula which contains the most expensive ingredients of their kind. For instance, he uses Vitamin B-6 which costs at the factory $550 a kilogram, which is less than half a gallon." [The senator forgot to say that his $550 worth of vitamin B_6 is enough for 125,000 bottles of Hadacol (half-pints at $1.25 a bottle).—ED.]

The Federal Trade Commission recently announced that the LeBlanc Corporation and its president had agreed to discontinue certain advertising misrepresentations concerning the therapeutic properties of Hadacol. In its report dated Sept. 5, 1950, the commission announced: "They agree to stop representing that 'Hadacol has any therapeutic value other than such as results from the vitamin B_1, vitamin B_2, iron and niacin it supplies, and then only when clearly limited to cases resulting from a deficiency of one or more of these nutritional elements." The stipulation also calls for discontinuance of the representation that Hadacol "has any dietary value except such as may result from providing vitamin B_1, vitamin B_2, iron and niacin, and one-third the minimum daily adult requirements of calcium and phosphorus." The firm further agreed to "cease and desist from exaggerating the frequency with which any disease, symptom or condition is due to a deficiency of vitamin B_1, vitamin B_2, iron or niacin. Other representations to be discontinued under the provisions of the stipulation are that Hadacol assures good health, restores youthful feeling and appearance, does not contain drugs or influences health without the use of drugs. . . ." However, currently used testimonials leave the impression which the Federal Trade Commission said could not be gained by flat advertising claims.

Possibly this Federal Trade Commission announcement had something to do with the new theatrical twist in the lay promotion of Hadacol. Early in the game testimonials were used to claim its value in anemia, arthritis, rheumatism, asthma, diabetes, epilepsy, heart trouble and high blood pressure, low blood pressure and gallstones, paralytic stroke, ulcers, tuberculosis and even cancer. Now it is being proclaimed to the gullible by means of a gigantic "medicine show," complete with Hollywood stars.

A Chicago newspaper recently carried an advertisement headed: "Wanted, a Parrot." The advertisement went on to say:

> "The LeBlanc Corporation, of Lafayette, La., makers of HADACOL, a vitamin and mineral formula, are seeking the services of a parrot that will say distinctly, many times a day, 'Polly wants HADACOL.'
>
> "The owner of such a bird, if selected, will be given a reasonable compensation on a contract basis. The owner and the parrot will travel throughout the nation in a limousine with the parrot's named engraved in gold on the door and will stay at only the best hotels. The parrot will be furnished a gold cage and its life insured.
>
> "The parrot will visit large drug stores, perform at jobber's salesmen meetings, conventions, etc., and may be presented on radio and television. The LeBlanc Corporation has a triple A high credit rating. For further information contact Hedrick & Towner Advertising Agency, 3704 Travis St., Houston 6, Texas."

The Bureau has no knowledge at present of the success of the senator's quest for a parrot. But the Bureau hopes that he is more circumspect in selecting a parrot than he was in the selection of his "clinical research director."

MISCELLANY

Health Problems in Alaska.—Dr. Jack C. Haldeman, medical officer in charge of the Arctic Health Research Center, said in an address before the recent Alaskan Science Conference that (on the basis of reported causes of death) accidents, alcoholism, suicides and homicides, as a group, accounted for 32 per cent of the deaths in Alaska among the white population during the five year period ending December 1949. By comparison, in 1948 only 9 per cent of all deaths in the United States as a whole were attributed to these causes. Alcoholism was reported as the immediate cause of death among the white population 20 times as often in Alaska as in the States and eight times as often among the nonwhite group. Tuberculosis was reported as the cause of death on 43 per cent of all death certificates for Indians, Eskimos and Aleuts in Alaska in 1946, 10 times as often as in the United States as a whole, and the combined pneumonia-influenza death rate was almost four times that of the States.

"In 1938, I observed a whooping cough outbreak in the lower Kuskokwin delta area which literally affected every man, woman and child in several villages. Another whooping cough outbreak in a village of about 150 inhabitants resulted in 9 deaths." It is paradoxical that the low temperature areas of the world, which contain the fewest persons per square mile, are plagued with those major health problems usually associated with overcrowded living conditions, Dr. Haldeman said. Even in the spacious North it is not uncommon for an Eskimo family of 12 to be living in a single 9 by 9 foot hut in order to conserve heat. The attack rate of diseases spread directly from person to person is understandably high under such conditions, whether the population sample is taken from the slums of a metropolitan area or from an Eskimo village. Diseases that are spread chiefly through discharges of the intestinal tract, although less frequently reported as the immediate cause of death, represent a major cause of morbidity in Alaska.

Dr. Haldeman said it would appear that the incidence of syphilis is lower in Alaska than was previously thought. Serological surveys conducted in some villages have failed to disclose a single person infected with syphilis. However, morbidity reports of the Alaska Department of Health indicate that, once syphilis is introduced into a village, it frequently assumes epidemic proportions.

Other health problems in Alaska include broad fish tapeworm infection, trichinosis, phlyctenular keratoconjunctivitis and nutritional deficiencies. Tularemia, botulism, brucellosis and rabies are present in the Territory.

"Little scientific information is available concerning basic differences in racial pathology among the white, Indian, Eskimo and Aleut populations," Dr. Haldeman said. "We have no way of knowing whether the high tuberculosis mortality rate among the latter groups should be attributed simply to a higher degree of racial susceptibility or to a combination of factors, such as exposure to massive doses of tubercle bacilli, crowded living conditions, poor nutrition, recurrent gastroenteric diseases and parisitism. What about the devastating effects of other diseases? What diseases existed among the Eskimos and Indians prior to the coming of the white man? It would seem that here are but a few of the areas where the public health worker and the anthropologist could well collaborate in worth while research."

In the first long range study of its kind by a resident staff, the Arctic Health Research Center is seeking to improve the health of the people of Alaska and to find answers to basic questions about physical, mental and emotional adjustments to low temperature environments. The program is entering its third year.

BUREAU OF LEGAL MEDICINE AND LEGISLATION

MEDICOLEGAL ABSTRACTS

Evidence: Reliability of Tests for Sterility.—This was an action by the petitioner against her husband for support of herself and the minor child of the parties. The hearing was held in the domestic relations court of the City of New York.

The parties hereto intermarried on Sept. 28, 1940, and that relationship has never been terminated by judgment of divorce, separation, annulment or dissolution. The respondent, however, asserted complete exoneration from any duty of support on the ground that because of claimed sterility he is not the father of the petitioner's child born June 3, 1949. The sole disputed question for determination, said the court, is whether the evidence adduced by the respondent suffices to overcome the time-honored presumption that a child born to a married woman during coverture was procreated by her husband.

The blood-grouping tests which respondent requested did not establish definite exclusion; the respondent's seemingly sincere belief that he is not the father of the child and his consequent resistance to any order of support derive wholly from certain other medical testimony. A clinical laboratory technician (not a physician) testified that his June 7 and Oct. 20, 1948, examinations of purported specimens of respondent's seminal fluid showed complete absence of spermatozoa. A qualified urologist also testified that his microscopic examination of respondent's seminal fluid on Nov. 24, 1948 and a second examination after sedimentation and centrifugal processing disclosed azoospermia, which he attributed to a blocking of the epididymis ducts from prostatitis or a previous infection. He further testified that the scar tissue he observed indicated, in his opinion, that the November 24 absence of spermatozoa had existed for at least 30 days and perhaps 60 days. However, both he and another urologist called by respondent admitted that it was medically possible that the sterile condition observed on Nov. 24, 1948 might not have existed at the inception of petitioner's pregnancy in August or September, 1948.

If the blood-grouping tests in this case had established definite exclusion, said the court, and if those tests had been shown to have been accurately and completely made, such evidence would have served to overcome the presumption of legitimacy of a child born to a married woman. However, the court continued, not only were the blood-grouping tests inadmissible because they did not establish definite exclusion but also quite different considerations govern a plea of sterility. Blood-grouping, nonpaternity test technics have now been developed to the point of scientific certainty. Not so, said the court, in the field of sterility, which is still in the nascent stage and fraught with uncertainties. Quoting from "Disputed Paternity Proceedings" (second edition), by Sidney B. Schatkin, the court said, "If the defendant raises the defense of sterility, it must be based on the examination of his seminal fluid by a scientific expert in the field of male reproduction, to determine the presence or absence of motile spermatozoa. . . . If the expert testifies to a state of sterility on the date of the examination, that testimony is not sufficient. The expert must give his opinion as to how long that condition existed and, specifically, whether it existed on the date of the alleged act of intercourse. . . . A man, of course, may be examined today and found to be sterile. The crucial question is: Was he sterile at a given previous period of time?" The court also quoted from "Fertility in Men" by Dr. Robert S. Hotchkiss, a leading expert: "Our factual knowledge has not yet reached the point where we can unreservedly state that certain sterile men will never regain their fertility. . . . The risks of dogmatic declarations are evidenced by contemplation of the repercussions which might follow a statement to the husband that he is 'permanently sterile.' Should he by some unusual method regain or improve his fertility and a pregnancy take place, he will probably doubt his paternity. Such an unjustified suspicion may dissolve a marriage."

As against the inconclusive medical testimony, on the one hand, there are on the other, an accumulation of countervailing factors, namely, the strong presumption of the child's legitimacy, the conceded continuance of marital intercourse between the parties until several months after the child's birth, respondent's payment of the confinement expenses, his claiming the child as a dependent for income tax purposes, the belatedness of his disclaimer of paternity, the dearth of identification of any paramour or proof of any inclination of petitioner to infidelity, and petitioner's own positive and credible testimony. Accordingly the court found that the allegations of the petition were sustained and that the respondent was liable for the support of his wife and the child.—*Houston v. Houston, 99 N.Y.S. (2d) 199 (New York 1950).*

Charitable Hospitals: Extent of Tax Exemption.—A number of California hospitals filed suits to recover taxes which they contended should not have been assessed and collected in view of the tax exempt status of hospitals. All the suits were consolidated for trial, and, after a hearing in the superior court, the various parties appealed and cross appealed to the district court of appeals, second district, division one, California. A further appeal was then taken to the Supreme Court of California.

The issue raised in these cases was as to the tax liability of the hospitals in regard to certain portions of their property used for the purpose of providing housing for the hospital interns, student nurses and other essential employees, for a training school for student nurses, for recreational facilities for student nurses, interns and residents, for housing a "thrift shop" in conjunction with charitable purposes and for certain portions of property on which buildings to be used for housing student nurses were under construction at the time of the assessment. The opinion of the district court of appeals (*J. A. M. A.* **141**:348 [Oct. 1] 1949) held that none of the above property was subject to general property taxes. The Supreme Court held otherwise, however, regarding the last two items.

Hospital property used to house a "thrift shop," said the Supreme Court, is not entitled to the benefit of the tax exemption. The "thrift shop" is located on the lower floor of the hospital building, "where donated clothing and furnishings are sold" and the "entire proceeds . . . are devoted to the maintenance of the Free Children's Clinic maintained jointly by the [hospital] and [a Community Chest] agency . . . deemed by the [hospital's] board of directors to be a charitable use." Such enterprise, laudable as its purpose manifests it to be, cannot escape classification as an independent undertaking to raise revenue, and it cannot be said to have been incidental to, and reasonably necessary for, the accomplishment of hospital purposes. In truth, the Supreme Court continued, it was conducted solely for revenue purposes as distinguished from hospital purposes. While the profit or gain derived from its operation benefited the hospital in providing support for its clinic, such consideration must be viewed in the light of the express statutory proviso that "property used exclusively for . . . hospital . . . or charitable purposes is exempt from taxation if . . . the property is not used or operated by the owner or by any other person for profit regardless of the purposes to which the profit is devoted." Such plain language prohibits the allowance of the exemption claim here in question.

The Supreme Court also considered the question of whether property on which are located buildings under construction and intended for use in the housing of student nurses is within the welfare exemption. On the assessment date the building on each of two pieces of property was approximately 85 per cent completed, was designed to be used exclusively as a dormitory and residence for student nurses and was in fact placed in use for the designated purposes a few months later. The pertinent

statute, said the Supreme Court, unequivocally requires that the property be "used" for the enumerated purposes. Such express limitation, making use the focal point of consideration, contemplates actual use as differentiated from an intention to use the property in a designated manner. It has been generally so held in the construction of kindred exception laws in other jurisdictions, said the Supreme Court. Under no theory of construction could a building in the course of erection be viewed as being used for any purpose. Considerations attesting to the exercise of the institution's good faith in carrying out its building program are wholly immaterial under the welfare exemption law, where the language plainly makes use of the property the basis of the exemption, and manifestly an incompleted building cannot meet that condition.

Accordingly the Supreme Court held that property used for a thrift shop and property on which buildings are still under construction is not subject to the welfare exemption provisions but that property used for the purpose of providing housing for hospital interns, student nurses and other essential employees, for a training school for student nurses and for recreational facilities for student nurses, interns and residents is exempt from general property taxes.—*Cedars of Lebanon Hospital v. Los Angeles County 221 P (2d) 31 (Calif. 1950).*

MEDICAL MOTION PICTURES

The Quiet One. 16 mm., black and white, sound, showing time 75 minutes. Prepared by Viola Bernard, M.D., Psychiatric Consultant with the Technical Assistance of Wiltwyck School for Boys, Inc., Robert L. Cooper, Executive Director and Nathan Stillman, Director. Produced in 1948 by Film Documents, New York. Procurable on rental or lease from Athena Films, Inc., 165 West 46th Street, New York.

This motion picture was made in New York City and the Wiltwyck School for Boys in Esopus, N. Y., to show the effects of environment in shaping patterns of delinquency and the therapy used by the Wiltwyck School in readjusting a product of such environment to a normal childhood. The film portrays the story of a 10 year old boy who had the misfortune to be born into a family that resented his existence and left him to shift for himself. It vividly portrays the hopeless struggle that builds up in the mind of a child continually denied the feeling of being wanted. Fighting loneliness, boredom and depression, he habitually skips school and eventually drifts into delinquency. The child is sent to a correction school for wayward boys staffed by experienced counselors under the direction of a psychiatrist. The job of emotional rehabilitation is what makes this film so fascinating to students of human behavior.

This is a remarkable film both for its artistry and for the soundness of the psychological principles it sets forth. Psychological validity is never sacrificed for the sake of the story, yet it is the story that holds one's interest. The producers are to be commended for not oversimplifying the vastly complicated situation of an unloved child struggling to relate himself to his surroundings. Even when the boy gets into the school where he is given the best of care and the most favorable environment, he still struggles and even runs away. The film brings out subtly how counselor, social worker, psychiatrist and teacher in the school worked together in bringing the boy to emotional health. The discussion group leader which should accompany this film might do well to point out that the "loneliest child is everywhere." The unloved child stands out more vividly in blighted areas which point up his loneliness, but he is not altogether a product of slum conditions nor do good neighborhoods guarantee emotional well-being.

The producers resisted the temptation to moralize or blame anyone for the tragic difficulties confronting the boy, and that, too, strengthens the picture. The groups who might profit from this film are medical students or residents in pediatrics or psychiatry, persons connected with child care institutions as staff or volunteer workers, social workers and nurses preparing for public health work or pediatrics and teachers working with retarded children. With careful interpretation, the film would have great meaning for parents. It would be an excellent film to use with civic-minded groups, such as Rotary, Kiwanis or Boy Scout leaders, especially as a means of giving them a picture of unmet social needs. The film would be of interest to anyone working with children, whether as a parent, a teacher or a member of an institutional staff. It could be the basis for a series of discussions in a class on child development. The photography, narration and direction are outstanding.

New Voices. (technical version), 16 mm., sound, half black and white, half color, showing time 14 minutes. Produced in 1949 by and procurable from Cleveland Hearing and Speech Center, Inc., 11206 Euclid Avenue, Cleveland 6.

This motion picture portrays the chance discovery of cancer of the larynx, the subsequent confirmation by diagnosis and the preoperative training by both the surgeon and former patients. The postoperative visits by persons who have learned the new way to speak, the formal training program at the speech clinic and the first visit to the Lost Chord Club meeting, give encouragement and training instructions in the development of the new voice.

The film shows in detail the facets which are important in case management, including the careful preparation of the patient for his postoperative life with explanations from the surgeon and demonstrations of successful rehabilitation by contacts with the actual case. A section of the film illustrates the surgical procedure. The postoperative rehabilitative program is explained, showing the stages in the training and the final successful adjustment of the case.

As a presentation of a successful case, the film is well done. It is a sensitive presentation of the major steps in rehabilitation as well as of the finer points involved in the psychological adjustment. The film is excellent for showing to medical groups both specialists and general practitioners and to types of rehabilitation workers and psychologists. This film is produced in two versions. The technical version, which contains a color sequence showing the laryngectomy operation, is intended for use only in medical schools and for professional audiences of nurses or speech therapists. The training version does not contain the operation sequence and is intended for showing to preoperative and postoperative patients. A 19 page training manual is sent with each film. The photography and narration are satisfactory.

NEW MOTION PICTURE ADDED TO A.M.A. FILM LIBRARY

The First Heart Beats and the Beginning of the Circulation of Blood in the Embryo. 16 mm., black and white, silent, 792 feet (2 reels), showing time 32 minutes. Prepared in 1940-1950 by Dr. Bradley M. Patten and Dr. Theodore C. Kramer, Department of Anatomy, University of Michigan, Ann Arbor. Procurable on loan (service charge $2) from the Committee on Medical Motion Pictures, American Medical Association, 535 North Dearborn Street, Chicago 10.

Part I shows the development of a chick heart by fusion of the paired primordia, the first twitches which are later to become the heart beat, the development of blood islands and, most spectacular of all, the first truly circulatory movements of the blood plasma bearing the first blood corpuscles. Part II is concerned largely with the physiological aspects of the primitive heart beat and beautifully shows the experiments whereby the region of the heart about the sinus venosus is shown to be dominant over the atrial and ventricular regions. The results of transection experiments are demonstrated in order to show that conduction in the heart at that stage is not yet dependent on a single conducting bundle.

The film achieves distinction as a contribution to science and to pedagogy. The first part will be valuable to classes in embryology, both at the medical school level and the college level. The second part will be more meaningful to medical students in connection with the course in cardiovascular physiology. The photography is remarkably good. The diagrams and subtitles are effectively used in such a way that they do not come between the audience and the documentary material being shown.

MEDICAL LITERATURE ABSTRACTS

AMERICAN

A.M.A. Archives of Neurology & Psychiatry, Chicago

64:491-606 (Oct.) 1950

*Surgical Therapy of Temporal Lobe Seizures. W. Penfield and H. Flanigin.—p. 491.
Patterns in Allesthesia and Their Relation to Disorder of Body Scheme and Other Sensory Phenomena. M. B. Bender and M. Nathanson.—p. 501.
Effect of Treatment on Excretion of 17-Ketosteroids in Patients with Mental Disease. M. D. Altschule and B. H. Parkhurst.—p. 516.
Cerebrospinal Fluid in Methyl Alcohol Poisoning. E. R. Reiner.—p. 528.
Tetraethylammonium Chloride in Treatment of Multiple Sclerosis. H. Arkin, I. C. Sherman and S. L. Weinburg.—p. 536.
*Frequency of Multiple Sclerosis in Greater New York. L. V. Chiavacci, H. Hoff and N. Polvan.—p. 546.
Histologic Observations on Supradiaphragmatic Portions of Vagus Nerves. E. A. Gaston and C. G. Tedeschi.—p. 554.
Serum Neuritis: Report of Two Cases and Brief Review of Syndrome. K. R. Woolling and J. G. Rushton.—p. 568.

Temporal Lobe Seizures.—Penfield and Flanigin discuss the localization of the discharge in seizures. In essential epilepsy the discharge originates in a centrally placed zone of gray matter in the diencephalon, midbrain and pons that is connected with both cerebral hemispheres. The electroencephalogram demonstrates bilaterally synchronous 3 per second spike and slow wave complexes. Discharge occurring in the cerebral cortex may produce a wide variety of symptoms, depending on the function of the area in question. If the focus is buried deep beneath the temporal lobe, electrodes on the scalp may fail to detect the spike discharges, but the electroencephalographer may report bilaterally synchronous alterations of brain waves that have been set up because, apparently, the spike focus under the temporal lobe is firing into a rhythmic mechanism within the higher brain stem. This paroxysmal dysrhythmia may take the form that has been described as psychomotor. The authors discuss temporal lobe seizures. The commonest temporal aura is a sensation in the abdomen, epigastrium, thorax or throat. Cephalic aureas and auditory, labyrinthine and olfactory aureas are frequent. Illusions of perception may occur. These phenomena may be a prelude to loss of consciousness or alteration in consciousness without convulsion and without loss of motor control. These are states of confusion and amnesia that may be called behavioral automatism or psychomotor state. The authors operated on 68 patients who had temporal lobe seizures. In seven cases exploration only was carried out, because the origin of the seizures could not be recognized. No excision was attempted, and none of these patients was relieved of his attacks. An infiltrating tumor was removed in five cases. In 55 cases an atrophic or stationary epileptogenic lesion of the cortex was excised. Of the 55 patients, 51 have been followed up to the present time. There was no improvement in seven and slight improvement in four. Improvement of 50 per cent or better was obtained in 13 cases. In 13 patients cure was preceded by only one or several attacks, and 14 patients were cured with no further attacks. The authors conclude that temporal lobe seizures produced by focal lesions may be treated by surgical ablation.

The Association library lends periodicals to members of the Association and to individual subscribers in Continental United States and Canada for a period of five days. Three journals may be borrowed at a time. Periodicals are available from 1940 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied with stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted.

Frequency of Multiple Sclerosis in New York.—Chiavacci and his co-workers made a survey of the cases of multiple sclerosis in New York. Their material was collected from most of the larger hospitals in greater New York by use of the pertinent data from all available case histories of the past 10 years. Case reports containing doubtful diagnoses were omitted. It was believed that a survey in New York would be especially interesting in view of the fact that the city has one of the largest and most racially varied populations in the world. Living and nutritional conditions, on the other hand, may be said to be more uniform there than elsewhere. A total of 4,898 patients were investigated. The distribution of the disease between the sexes was about equal. The incidence of multiple sclerosis among the white population was found to be about 6 in 10,000; whereas that for Negroes was only 1.4 in 10,000. Since the disease is rarely encountered in Italy and the South American countries, it was interesting to observe that the Italians of New York and the South American population showed the same incidence as other groups. The age distribution of multiple sclerosis coincided with the observations of other authors. Early onset of the disease indicated a better prognosis for remission than later onset, which was associated with a greater tendency to a slowly progressive or stationary course. Allergic conditions were not more frequent among patients with multiple sclerosis than among those with other diseases. The influence of pregnancy, abortion, operation or injury on the onset of the disease could not be confirmed. The age at the time of death of patients with multiple sclerosis did not deviate much from the average mortality figures for the various decades, and most deaths occurred from intercurrent diseases rather than from multiple sclerosis.

A.M.A. Archives of Ophthalmology, Chicago

44:499-634 (Oct.) 1950

Pseudoglaucoma. H. A. Blazar and H. G. Scheie.—p. 499.
Repair of Orbital Deformities with Glass Wool: Follow-Up Report. A. G. DeVoe.—p. 514.
Determination of Volume of Posterior Chamber of Rabbit's Eye. R. L. Copeland and V. E. Kinsey.—p. 515.
Intractable Postoperative Diplopia. G. L. Tabor Jr.—p. 517.
Studies of Depth of Anterior Chamber of Eye in Primary Glaucoma. B. Rosengren.—p. 523.
Retinal Capillary Lesions in Malignant Hypertension. D. Wexler and G. Branower.—p. 539.
Nystagmus: Its Diagnostic Significance. E. B. Spaeth.—p. 549.
Preparation of Ophthalmic Solutions with Special Reference to Hydrogen Ion Concentration and Tonicity. F. N. Martin Jr. and J. L. Mims.—p. 561.
*Human Infection with Newcastle Virus of Fowls. A. H. Keeney and M. C. Hunter.—p. 573.
Physiologic Chemistry of the Eye: Review of Papers Published During 1949. V. E. Kinsey.—p. 584.

Human Infection with Newcastle Virus of Fowls.—According to Keeney and Hunter, Newcastle disease, or avian pneumoencephalitis, is a highly communicable virus disease of fowls. Diseased animals discharge the virus in their oral and nasal secretions and in their feces. Eggs have been shown to contain the virus and to constitute another potential source of human infection. There was contact with sick poultry or Newcastle virus in each of the 33 cases so far reported. Incubation periods varied from a few hours to two days, and all patients recovered in five days to two weeks without sequelae. Most of the patients were laboratory workers, kitchen personnel, poultry feed salesmen or veterinarians. In one case an embryonated chick egg inoculated 48 hours previously with a known strain of Newcastle virus was accidentally crushed and the material splashed over the worker's face, arms and chest. The man immediately washed his face and hands, autoclaved his clothing and scrubbed under a hot shower. His eyes were rinsed in the shower and during the rest of the day irrigated

hourly with boric acid solution. The following morning the conjuntiva was red, but only scant secretions were present. Headache, backache and fever developed. On the second day conjunctival hyperemia was still about the same and a few pinpoint epithelial infiltrates were present in each cornea. On the third day both eyes continued to itch and water, but there was a reduction in conjunctival hyperemia and papillary hypertrophy. On the fourth day excess secretions had subsided almost entirely, but a preauricular lymph node became palpable and was tender for three days. During the next two weeks the injection and pebbly roughness of the conjunctiva gradually subsided. The pattern of Newcastle disease was reflected in both the white blood cell count and the serum antibody response. Aureomycin borate drops and penicillin drops (5,000 units per cubic centimeter) were instilled hourly in the right and in the left eye, respectively. This medication was instituted on the first day of illness but was discontinued with subsidence of major symptoms on the fourth day. There was no indication that either had influenced the infection. Active virus was recovered from both eyes after this treatment. Bacterial infection was excluded in this case, and virus material isolated from the conjunctiva and the blood stream was identified as Newcastle virus.

American Heart Journal, St. Louis

40:485-646 (Oct.) 1950

Variations in Duration of Phases of Cardiac Cycle in Normal Hearts as Studied by Electrokymograph. K. Willis, E. Eddleman Jr., J. K. Acker and others.—p. 485.

Effect of Posture on Cardiac Cycle, Posteroanterior Cardiac Diameters, and Apparent Stroke Volume as Studied by Electrokymograph. E. E. Eddleman Jr., K. Willis and H. E. Heyer.—p. 504.

Observations on Genesis of Electrocardiogram. R. H. Roseman.—p. 522.

Left Ventricular Cavity Potentials in Induced Left Bundle Branch Block Studied with Esophageal Leads. A. A. Sandberg, J. Wener and L. Scherlis.—p. 531.

*Significance of Q_{aVF} in Diagnosis of Posterior Infarction. P. N. G. Yu, and T. M. Blake.—p. 545.

Course of Excitation Wave in Patients with Electrocardiograms Showing Short P-R Intervals and Wide QRS Complexes (Wolff-Parkinson-White Syndrome). A. Grishman, I. G. Kropp and M. F. Steinberg.—p. 554.

Value of the aV Limb Leads and V Chest Leads (V_{4R} to V_7) in Routine Clinical Electrocardiography. R. H. Rosenman, E. Silber, L. N. Katz and B. Shorr.—p. 573.

Electrocardiographic Study of Intramuscular Quinidine Lactate. J. S. Feibush and D. Greenberg.—p. 585.

Antidotes to Ventricular Fibrillation Induced by Mercurial Diuretics. B. N. Craver, F. F. Yonkman and B. R. Rennick.—p. 590.

Congenital Aortic Atresia. I. W. Monie and A. D. J. DePape.—p. 595.

Myocardial Infarction Due to Syphilitic Coronary Ostial Stenosis. W. B. Scharfman, J. B. Wallach and A. Angrist.—p. 603.

Significance of Q_{aVF} in Posterior Infarction.—Yu and Blake point out that many investigators have corroborated Pardee's discovery of the diagnostic importance of a large Q wave in lead 3 in coronary artery disease and posterior infarction. A Q wave in lead 3 conforming to Pardee's criterion may be present in normal persons and is usually indistinguishable from that seen in posterior infarction. This large Q wave in normal persons is mainly due to the transverse position of the heart. Some authors maintain that the presence of a significant Q wave in the unipolar leg lead (V_F or aV_F) is helpful in deciding the significance of a large Q wave in lead 3. The presence of a significant Q wave in the V_F or aV_F leads strongly suggests that the quality of the Q wave in lead 3 is due to a posterior infarction and not to the position of the heart. More recently it has been stated that criteria derived from the unipolar limb leads are not dependable in the diagnosis of posterior infarction. The authors made a comparative study of Q waves in leads 2, 3 and aV_F in 54 patients with posterior infarction and 55 patients without infarction. A significant Q wave in lead 3 was present in all cases with or without infarction. On the other hand, a significant Q wave in lead aV_F was present in 91 per cent of patients with posterior infarction and in only three of the 55 patients without infarction. The authors believe that the presence in an adult of a Q wave in lead aV_F with a voltage of at least 25 per cent that of the R wave in lead aV_F and a duration of 0.04 second or more may indicate the presence of a posterior infarction. The use of the unipolar leg lead appears to aid in the differentiation of the normal and abnormal Q wave in lead 3 and therefore helps in establishing or excluding the diagnosis of posterior infarction.

American Journal of Medical Sciences, Philadelphia

220:357-476 (Oct.) 1950

*Clinical Orbitonometry. J. H. Means and J. B. Stanbury.—p. 357.

*Propylthiouracil in Thyrotoxicosis: Alternate Cases Treated Medically and Surgically. N. Taylor, A. Large and P. Noth.—p. 362.

Observations on Prolonged Medical Management of Toxic Diffuse Goiter with Thiouracil and Propylthiouracil. S. U. Greenberg and M. Bruger.—p. 373.

Intravenous Use of Quinidine, with Particular Reference to Ventricular Tachycardia. A. H. Clagett Jr.—p. 381.

Chloromycetin Treatment of Typhoid Fever: Report of Two Cases. G. P. Wiedman and S. S. Paley.—p. 389.

Chronic Schistosomiasis Japonica: Diagnosis by Rectal Biopsy with Description of Sigmoidoscopic Abnormalities. L. W. Hamrick Jr., E. A. Cleve and R. P. Carson.—p. 393.

Oxygen Therapy of Bundle Branch Block. J. Levy.—p. 400.

Rutin Therapy in Diffuse Capillary Bleeding: Ineffectiveness When Fragility Tests are Normal. W. H. Glass.—p. 409.

Precipitin Reaction of Serum from Cases of Rheumatoid Arthritis with Homologous Connective Tissue Extracts. J. Lansbury, W. R. Crosby and C. T. Bello.—p. 414.

Copper Therapy of Rheumatoid Arthritis. T. L. Tyson, H. H. Holmes and C. Ragan.—p. 418.

Multiple Sclerosis: Correlation of Its Incidence with Dietary Fat. R. L. Swank.—p. 421.

Effect of Vitamin B_{12} on Pain in Nutritional Neuropathy. W. B. Bean, M. Franklin and A. L. Sahs.—p. 431.

Intradermal Tests in Diagnosis of Certain Infectious Diseases. H. Beerman and N. R. Ingraham Jr.—p. 435.

Antihistaminic Drugs and Common Cold: Critical Review. N. D. Fabricant.—p. 464.

Clinical Orbitonometry.—Means and Stanbury made 200 measurements of the repressibility of the eye into the orbit on 53 patients with the aid of an instrument devised by Copper of the University of Leiden, Holland. Some of the patients had no evidence of eye disease; others had various ocular manifestations of toxic diffuse goiter. Copper's orbitonometer consists of a contact shell, a bridge and a dynamometer. The contact shell has a small plastic cuff that can be affixed to the anterior surface of the eyeball, which has been anesthetized with procaine hydrochloride. The instrument is simple to use. Reproducible data are quickly obtained without risk or great discomfort to the patient. Experience suggests that orbital resistance is increased in the active phase of the ophthalmopathic types of toxic diffuse goiter, is diminished in the inactive phase of that disease and is little changed in ordinary hyperthyroidism. The instrument makes it possible to follow the course and severity of Graves' ophthalmopathy in a quantitative fashion. The orbitonometer may be helpful in the early differential diagnosis of the benign and the malignant types.

Propylthiouracil in Thyrotoxicosis.—Taylor and co-workers report on 52 patients with hyperthyroidism, 37 of whom were followed up and studied for a sufficiently long period of time to permit conclusions. The 52 patients were subdivided in four groups: 18 patients with diffuse toxic goiter treated by thyroidectomy, 23 with diffuse toxic goiter treated medically, seven with nodular goiter treated by thyroidectomy and four with nodular goiter treated medically. The toxicity was high, with basal metabolic rates above +50 per cent in more than two thirds of the patients. Complications of thyrotoxicosis or associated diseases occurred in 43. Alternate patients with diffuse toxic goiter were treated medically and by thyroidectomy. Prolonged periods of propylthiouracil treatment were required in the majority of cases, possibly due to the large number of associated diseases, the large number of complications or the high level of toxicity. The average period of treatment required to bring the basal metabolic rate to normal was almost one year in the cases of nodular goiter and

about five months in the cases of diffuse goiter. The average dose of propylthiouracil required to bring the basal metabolic to normal or to perform operation was 37.8 and 29.8 Gm., respectively, in patients with diffuse goiter and 85.6 and 77.6 Gm., respectively, in patients with nodular goiter. Many of the medically treated patients died. Only three of the remainder have normal basal metabolic rates without continuing treatment. There was no death among the patients treated surgically, and the satisfactory results obtained are thought due to the reduction of the severe toxicity in patients who were poor risks by prolonged preparatory treatment with propylthiouracil. Agranulocytosis occurred in one patient treated elsewhere with antithyroid drugs. Toxic manifestations from propylthiouracil did not otherwise constitute a problem. A significant increase in exophthalmos occurred in eight of the 52 patients receiving propylthiouracil. There was no significant progression of exophthalmos in any case postoperatively. Definite regression following thyroidectomy occurred in four instances. On the basis of the observations in this small controlled series of cases of hyperthyroidism, the authors are inclined to favor the continued use of subtotal thyroidectomy as the standard treatment for diffuse goiter with hyperthyroidism. They advise operation on all patients who are being given antithyroid drugs and show any tendency toward progressive exophthalmos.

American J. Obstetrics and Gynecology, St. Louis

60:471-710 (Sept.) 1950. Partial Index

*Some Observations on Relations of Estrogens and Progesterone to Contractions of Nonpregnant and Pregnant Human Uterus. J. S. Henry, J. S. L. Browne and E. H. Venning.—p. 471.

Postpartum Blood Loss: Analysis of 6,000 Cases. J. R. Vant.—p. 483.

Review of 500 Elective Operations for Pelvic Prolapse on Women over Age of 60 Years. A. C. G. Frost.—p. 489.

*Arteriosclerotic Pregnancy Toxemia. J. L. McKelvey.—p. 510.

*Contribution to Study of Etiology and Prevention of Cancer of Cervix of Uterus. F. Gagnon.—p. 516.

Irregular Shedding of Endometrium. J. L. McKelvey.—p. 523.

Status of Internal Podalic Version in Obstetrics. E. B. Trowbridge.—p. 528.

Value of Vaginal Cytology in Observing Progress Under Radiation Treatment of Patients Suffering from Cancer of Cervix. G. C. Maloney.—p. 533.

Time of Ovulation: Correlation Between Basal Temperature, Appearance of Endometrium, and Appearance of Ovary. C. L. Buxton and E. T. Engle.—p. 539.

Measurement of Pain Intensity in Labor and Its Physiologic, Neurologic, and Pharmacologic Implications. C. T. Javert and J. D. Hardy.—p. 552.

Relationship of Disorders of Blood-Clotting Mechanism to Toxemia of Pregnancy and Value of Heparin in Therapy. B. C. Butler, H. C. Taylor Sr., and S. Graff.—p. 564.

Relationship of Endometrium to Chorioplacental Development and Its Gonadotrophin Output. E. C. Hughes, A. W. Van Ness and C. W. Lloyd.—p. 575.

Appraisal of Chorionepithelioma Based on Observations in 12 Cases. S. L. Siegler, J. M. Ravid and S. M. Tobin.—p. 586.

Emotional Aspects of Obstetrics and Gynecologic Disorders. A. J. Mandy, T. E. Mandy, R. Farkas and others.—p. 605.

Attempt at Desensitization of Women Immunized by Rh Factor: I. Use of Ethylene Disulfonate. W. C. Moloney.—p. 616.

Hyperrotation and Deflexion of Head in Breech Presentation with New and More Descriptive Terminology for Breech Presentation. R. A. Reis and E. J. DeCosta.—p. 637.

Clinical Study of 240 Infertile Couples. R. Frank.—p. 645.

Effects of Intravenous Injections of Ergonovine and Solution of Posterior Pituitary Extract on Postpartum Patient. W. J. Dieckmann, J. B. Forman and G. W. Phillips.—p. 655.

Estrogen Therapy by Implantation of Estradiol Crystals. G. T. Newman.—p. 661.

Diagnostic Culdoscopy. J. B. Teton.—p. 665.

Endometrial Biopsy: Comparison of Aspiration Curettage with Conventional Dilatation and Curettage. J. P. Palmer, W. F. Kneer and H. H. Eccleston.—p. 671.

Endometrial Hyperplasia Producing Syndrome Simulating Early Pregnancy. G. T. C. Way.—p. 675.

Estrogens and Progesterone in Contractions of Uterus.—Henry and his collaborators studied the relation of estrogens and progesterone to the contractility of the myometrium. They made tracings at different times in the luteal phase of normal cycles, cycles with deficient luteal phases and artificial cycles. They believe that the human uterus is capable of spontaneous myogenic contractions throughout the greater part of its life, that its activity is greatest during the years of sexual maturity and that it reaches maximum efficiency when it is called on to expel its contents, namely at the end of the cycle and at the end of pregnancy. The preparation for such maximal effort is almost certainly under the control of the same mechanism, that is, the synergistic action of estrogen and progesterone acting in normal proportions and for sufficient time. What actually sets the expulsive contractions in motion is still unknown. The authors know of no evidence that estrogen and progesterone are ever antagonistic in their effects on the uterus. The corpus luteum and the placenta secrete both hormones. Therapy that aims at replacement of luteal function in the cycle or in pregnancy must therefore combine estrogen and progesterone. Pregneninolone influences the activity of the myometrium and development of the endometrium in the way progesterone does, but it must be given in large doses for comparable effects to be produced. When the uterus has to expel its contents prematurely, as in abortion, the inefficiency of the mechanism is seen in the low pregnanediol output and particularly in the inadequate uterine musculature, which permits the dead products of conception to be carried for days, weeks and even months before they are expelled; and even then exploration of the uterine cavity is almost always necessary to ensure that it is empty. The authors think that this indicates an incomplete preparation of the uterine musculature for the great expulsive efforts rather than an inhibition of its contractions by progesterone.

Arteriosclerotic Pregnancy Toxemia.—McKelvey asserts that there are two types of hypertensive pregnancy toxemia. The preeclampsia-eclampsia complex has been given the attention that something dramatic always commands. The less dramatic permanent proliferative arteriolar hypertensive toxemia has not been accorded the study it demands. In a 12 month period in 1941-1942, there were 112 maternal deaths in Minnesota. Only four of these were due to eclampsia. In the same period about 500 women died as a result of a permanent hypertension, which began with a hypertensive pregnancy toxemia in the previous 10 years. Confusion has arisen because a variety of terms has been applied to this disease. Chronic nephritic toxemia was a misnomer, and its use did a serious disservice to an understanding of the problem. It has nothing to do with chronic parenchymatous nephritis. Essential hypertension of pregnancy is a better term, but it has defects. The clinical picture is that of a patient, often with a family history of hypertension, who becomes pregnant and develops a hypertensive toxemia. The blood pressure may not return to normal, and albuminuria may not disappear. These obstetrical patients are likely to be relatively young and subject to rapid progression of the disease. If a subsequent pregnancy occurs, a rise in blood pressure above the prepregnant level usually occurs in the early months. At least some of this increase disappears at the end of pregnancy. The permanent hypertension may take a variety of courses. Usually the vessels of the kidney and of the central nervous system show the severest changes. The prognosis is more favorable in women who do not become hypertensive until the later years of the reproductive period, in those in whom the disease has been present for a considerable time without too pronounced advance, in those who are not obese or who will control their obesity and particularly in those who go through the menopause with diastolic pressure at rest well below 110 mm. of mercury. Weight reduction, sodium restriction and sympathectomy are important factors in the treatment.

Etiology of Cervical Cancer.—Gagnon made gynecologic observations on a large number of nuns over a long period of years. A survey of the medical files of an annual average of 13,000 women, covering a 20 year period, was carried out in the records of a number of convents. This number of adult women corresponds to a city with a population of approximately 65,000 inhabitants. The comparative frequency of carcinoma of the cervix uteri and corpus uteri varies according to the statistics of different authors from between eight and five instances of the former disease for every one of the latter. There were 12 histologically verified cases of carcinoma of the

body of the uterus among the 13,000 nuns. Taking Meig's index of frequency of 6:1, there should have been 72 cases of cervical carcinoma, but not one was discovered. This would mean that in a city of about 65,000 inhabitants there would not have been a single case of carcinoma of the cervix uteri in 20 years. The author also investigated the records of treatment given at Montreal's Radium Institute for the past 20 years and those of the Radium Institute of Quebec, kept since the latter's foundation 12 years ago. Among 130 malignant tumors of all organs found in 3,280 nuns over a period of 20 years, there was not a single instance of cervical cancer. Carcinoma of the cervix may be rarely found in virgin women. Chronic cervicitis, particularly the inflammatory erosion, may exist in virgin women. Decreased incidence of cervicitis, if it is a causative agent, should, theoretically, bring about a decreased incidence of cancer of the cervix.

American Journal of Ophthalmology, Chicago

33:1325-1496 (Sept.) 1950

*Clinical and Experimental Observation on Use of ACTH and Cortisone in Ocular Inflammatory Disease. A. C. Woods.—p. 1325.
Chemistry of Pituitary Principles Acting upon Ocular Tension. A. A. Dietz, E. Schmerl and B. Steinberg.—p. 1349.
Glaucoma: Stastical Review of 816 Patients with 1,112 Glaucomatous Eyes. A. N. Lemoine Jr.—p. 1353.
Problem of Glaucoma. H. Elwyn.—p. 1373.
Separation of Diencephalic Centers Concerned with Pupillary Motility and Ocular Tension. E. Schmerl and B. Steinberg.—p. 1379.
Glaucoma: Some Social and Medical Aspects. D. Kravitz.—p. 1381.
Trephining Operations. J. A. Van Heuven.—p. 1387.
Visual Field as Aid to Prognosis in Glaucoma. A. Posner and A. Schlossman.—p. 1391.
Iridoschisis as Cause of Glaucoma. C. McCulloch.—p. 1398.
Nevus Flammeus Associated with Glaucoma. H. H. Joy.—p. 1401.
Lysozyme in Treatment of Ophthalmic Conditions. C. Hobart.—p. 1409.
Peripheral Choroiditis Simulating Retrolental Fibroplasia. R. D. Harley and R. W. Mather.—p. 1417.
Retardation of Wound Healing in Corneal Epithelium by Lanolin. J. C. Heerema and J. S. Friedenwald.—p. 1421.

ACTH and Cortisone in Ocular Disease.—Woods reports on pituitary adrenocorticotropic hormone (ACTH) as administered parenterally in the treatment of 14 patients with various ocular disorders. Cortisone was used topically in the eye in the treatment of eight additional patients. Five of the 14 patients who received the hormones parenterally remained unimproved. These included patients with syphilitic interstitial keratitis, juvenile retinitis exudativa (Coats' disease), nonsyphilitic keratitis (Cogan's syndrome) and retrolental fibroplasia. The nine patients who showed improvement after systemic treatment with these hormones included a patient with nongranulomatous iritis, one with disciform degeneration of macula secondary to subretinal hemorrhage, two with sympathetic ophthalmia (one with atropine sensitivity), one with sclerokeratitis with atropine sensitivity, one with tuberculous choroiditis with secondary glaucoma, one with nongranulomatous cyclitis and two with tuberculous uveitis and secondary glaucoma. The total dosage of pituitary adrenocorticotropic hormone was considerably in excess of 3,000 mg. and was continued for periods of over 40 days. The systemic administration of cortisone was usually continued for 10 days. In one case the total dose for this period was 1,280 mg. The beneficial effect of the parenteral administration of the hormones were a clearing of circumcorneal congestion and of the vitreous, circumscription of exudates and disappearance of subretinal edema. The beneficial results were invariably accompanied with a drop in the eosinophil count, often to the point of complete suppression. When cortisone is given locally by instillation in the conjunctival sac, there appears to be a subsidence of external inflammation and exudation, with resulting control of secondary glaucoma. It appears that local instillation of cortisone has little appreciable effect on exudation in the vitreous. In the majority of the conditions in which the blocking effect on inflammation was observed, there was some reason to suspect an allergic factor for the inflammatory reaction. Nongranulomatous iritis is believed to be due to bacterial hypersensitivity. The inflammatory phase in tuberculous disease is dependent on a hypersensitivity to tuberculoprotein. There is reason to believe that hypersensitivity of uveal pigment is a part of the symptom complex in sympathetic ophthalmia. Experimental studies confirmed the clinical observations. Although pituitary adrenocorticotropic hormone and cortisone block the inflammatory and exudative phases of the anaphylactic and allergic reaction, the evidence indicates that they have no effect on the underlying hypersensitive state.

American Review of Tuberculosis, New York

62:337-454 (Oct.) 1950

Effects of Cortisone on Development of Tuberculous Lesions in Guinea Pigs and on Their Modification by Streptomycin Therapy. D. M. Spain and N. Molomut.—p. 337.
*Effect of Neomycin on Tuberculosis in Guinea Pigs Infected with Streptomycin-Resistant Tubercle Bacilli. A. G. Karlson, J. H. Gainer and W. H. Feldman.—p. 345.
Angiocardiography in Artificial Pneumothorax. I. Steinberg, H. I. McCoy and C. T. Dotter.—p. 353.
Nicotinamide Therapy of Lingual Changes in Tuberculous Patients. E. L. Sevringhaus, S. Cohen, R. H. Gans and Sung-Nien Lu.—p. 360.
Cellular and Immunological Reactions in Rabbits Infected with Histoplasma Capsulatum. G. J. Scheff and I. M. Pfeifer-Scheff.—p. 374.
Tuberculosis of Heart: Review. W. C. L. Diefenbach.—p. 390.
*Sarcoidosis: Preliminary Report on Study of 350 Cases with Special Reference to Epidermiology. M. Michael Jr., R. M. Cole, P. B. Beeson and B. J. Olson.—p. 403.
BCG Vaccination in Sarcoidosis. H. L. Israel, M. Sones, S. C. Stein and J. D. Aronson.—p. 408.
Immunization Studies with Irradiated Tuberculosis Vaccines. R. W. Sarber, W. J. Nungester and F. D. Stimpert.—p. 418.
Emotional Factors in Pulmonary Tuberculosis. G. F. Fordham and L. J. Karnosh.—p. 428.
Thoracoplasty Failure as Indication for Resection in Pulmonary Tuberculosis. P. Ottosen, A. J. Beatty and W. W. Buckingham.—p. 434.

Neomycin in Tuberculosis.—Karlson and co-workers produced experimental tuberculosis in 32 guinea pigs by subcutaneous inoculation of streptomycin-resistant tubercle bacilli. Six animals were killed 21 days later, and grossly visible lesions of tuberculosis were observed on necropsy. The remaining animals were divided in three groups consisting respectively of 10 untreated control animals, six treated with 6 mg. of streptomycin daily and 10 treated with neomycin. Treatment was started on the twenty-first day of the infection. Neomycin was administered twice daily, with 2,000 units given for six days, 4,000 units for 18 days, 6,000 units for 23 days and 8,000 units for 30 days. The experiment was terminated after 77 days of treatment. The surviving animals were killed, and necropsy was performed. In contrast to the widespread destructive lesions seen in the untreated animals and in those treated with streptomycin, there were few grossly visible lesions in the animals treated with neomycin. Indications of repair and healing, such as fibrosis and calcification, were predominant on microscopic examination. Lesions of the renal cortex characterized by tubular destruction and cellular infiltration were seen in the kidneys of all the animals treated with neomycin. This demonstration of the therapeutic effect of neomycin warrants further studies to determine the optimal therapeutic dose, the optimal frequency of administration and the effect of the drug when used in combination with other antituberculous agents.

Sarcoidosis.—Michael and co-workers present a preliminary report on 350 patients with sarcoidosis. It was noted that most of these patients were born in southern and rural areas. Definite regional distribution of the etiological agent is not a new epidemiological feature. Persons from the South may be so constituted or so influenced by their environment that they respond to one or more etiological agents with the pathological picture of sarcoidosis. The possibility remains that the same environmental factor of the endemic area, such as soil, water, food or habits, may alter tissue reactions of the inhabitants to such an extent that the sarcoidosis picture results from an agent that would incite a different disease process away from this locale. Available data on incidence of positive or negative tuberculin reactions according to chief place of residence revealed a positive skin reaction to tuberculin in 26 of 56 patients who were born in the city or spent the major portion of their lives there. In contrast, only 25 of 107 patients who

were born and lived most of their lives in rural areas had a positive reaction. A negative skin reaction to tuberculin was often listed as a diagnostic feature of sarcoidosis, and this incidence may be related to the distribution of the disease predominantly in sections where negative skin reactions to tuberculin are commonly encountered, such as in rural areas. The previously observed predilection of sarcoidosis for the Negro race in the United States was also noted. It may be related to the regional distribution of the disease.

Anesthesiology, New York

11:517-650 (Sept.) 1950

Physiological and Physical Factors Governing Uptake of Anesthetic Gases by Body. S. S. Kety.—p. 517.
Intravenous Supplementation During Nitrous Oxide Anesthesia: Comparison of Demerol, Morphine and New Potent Analgesic Drug (15431). M. Brotman, S. C. Cullen and D. S. Wilkins.—p. 527.
Manually Assisted and Controlled Respiration: Its Use During Inhalation Anesthesia for Maintenance of Near-Normal Physiologic State—Review. W. G. Watrous, F. E. Davis and B. M. Anderson.—p. 538.
Preliminary Investigations of Carbon Tetrafluoride as Inert Diluent Gas to Prevent Explosions of Mixtures of Cyclopropane and Oxygen. C. S. Jones, A. Faulconer Jr. and E. J. Baldes.—p. 562.
Liver Function and Anesthesia. J. T. Hugill.—p. 567.
Study of Blood-Oxygen Saturation in Children Under Rectal Pentothal Anesthesia. B. E. Marbury.—p. 589.
Special Considerations in Selection and Employment of Anesthetic Agents and Methods in Infants and Children. M. D. Leigh and M. K. Belton.—p. 592.
Some Methods of Analysis and Determination of Anesthetic Agents. W. M. Strayer.—p. 599.
Regional Anesthesia with Tetracaine. J. J. Bonica.—p. 606.
Effect of Quinidine on Arrhythmias Induced by Cyclopropane and Cyclopropane-Epinephrine. R. A. Huggins, R. A. Morse, D. W. Chapman and L. F. Schuhmacher.—p. 623.

Arizona Medicine, Phoenix

7:1-72 (Oct.) 1950

Practical Recognition and Treatment of Cardiac Arrythmias. S. R. Elek.—p. 21.
Importance of Preoperative Evaluation of Patient for Proper Premedication and Choice of Anesthesia. J. B. Dillon.—p. 28.
Selection of Anesthesia for Cardiac Patient. A. G. Urry.—p. 33.
Differential Diagnosis of Hemorrhage from Upper Gastro-Intestinal Tract. H. N. Douds.—p. 36.

Canadian Medical Association Journal, Montreal

63:211-324 (Sept.) 1950

Newer Concepts of Etiology and Management of Idiopathic Ulcerative Colitis. S. A. Portis.—p. 237.
Homosexuality—Mental Hygiene Problem. S. R. Laycock.—p. 245.
Treatment of Acutely Intoxicated Alcoholics. H. W. Smith, G. L. McBroom and R. G. Bell.—p. 250.
Oral Penicillin Prophylaxis in Rheumatic Fever Patients. M. Brick, H. McKinley, M. Gourley and others.—p. 255.
Medical Aspects of Bone Disease with Particular Reference to Osteoporosis. R. P. Howard.—p. 258.
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Treatment of Syphilis. B. Kanee.—p. 269.
Amaurosis in Whooping Cough. N. W. Woyitka and J. V. Riches.—p. 272.
Antihistaminic Drugs. S. Leblond.—p. 274.
*Neurotoxicity of Dihydrostreptomycin. S. J. Shane and J. H. Laurie.—p. 277.
Fractures of Malar Bone and Zygomatic Arch. A. L. Murphy.—p. 279.
New Sedative Combination for General Practice. G. T. Novinger.—p. 281.
Acute Leukemia Treated with Folic Acid Antagonist. D. L. McNeil.—p. 284.

Neurotoxicity of Dihydrostreptomycin.—Shane and Laurie treated 21 patients with pulmonary tuberculosis with 2 Gm. of dihydrostreptomycin sulfate daily for 90 days. None of these patients showed evidence of vestibular dysfunction. Two patients developed severe hearing loss, one on the eighty-ninth day of therapy and one 24 days after the drug had been withdrawn. It therefore appears that dihydrostreptomycin is not as innocuous as previous reports have indicated it to be. It remains to be seen whether carefully performed audiometric tests would furnish the warning signal, which is lacking in the case of dihydrostreptomycin, by giving evidence of an earlier stage of cochlear nerve damage than is revealed by less exact tests of auditory acuity and the onset of clinical deafness.

Cancer, New York

3:757-944 (Sept.) 1950

Carcinoma of Breast: Recurrence and Survival in 203 Patients. A. H. Robnett, T. E. Jones and J. B. Hazard.—p. 757.
Surgical Treatment of Cancer of Lower Bowel. H. E. Bacon and I. Sauer.—p. 773.
Radioactive Phosphorus: I. In Treatment of Lymphatic Leukemia. H. D. Diamond, L. F. Craver, H. Q. Woodard and G. H. Parks.—p. 779.
Carcinogenic Action of Benzidine. S. Spitz, W. H. Maguigan and K. Dobriner.—p. 789.
Primary Diffuse Tumors of Meninges (So-Called Meningeal Meningiomatosis). B. K. Black and J. W. Kernohan.—p. 805.
Solitary Fibrous Mesothelioma of Peritoneum. A. P. Stout.—p. 820.
Embryonal Rhabdomyosarcoma of Head and Neck in Children and Adolescents. G. D. Stobbe and H. W. Dargeon.—p. 826.
Primary Carcinoma of Liver with Extensive Skeletal Metastasis and Panmyelophthisis. O. Auerbach and S. Trubowitz.—p. 837.
Steroid Excretion in Patients Receiving Antifolic Acid Compounds. E. B. Schoenback, J. Colsky and R. A. Lewis.—p. 844.
Studies on Mechanism of Action of Chemotherapeuic Agents in Cancer. A. Goldin, E. M. Greenspan, B. Goldberg and E. B. Schoenbach.—p. 849.
Studies on Role of Folic Acid in Leukemic Process. H. E. Skipper, J. B. Chapman and M. Bell.—p. 871.
Interference Between Certain Neurotropic Viruses and Transplantable Mouse Tumors. H. Koprowski and T. W. Norton.—p. 874.
Further Studies on Destructive Effect of Virus of Russian Far East Encephalitis on Transplantable Mouse Sarcoma 180. A. F. Moore and S. O'Connor.—p. 886.
Development of Malignant Lymphoma in Some of Young Rats Suckled by Mothers Receiving Methylcholanthrene by Stomach Tube Only During Lactation Period: Preliminary Report. H. Shay, S. Weinhouse, M. Gruenstein and others.—p. 891.
Effect of Azaguanine on Mitosis in Normal and Neoplastic Tissues. D. M. Shapiro, R. Weiss and A. Gellhorn.—p. 896.
Co-operative Effects of Endocrinological Factors and Processes of Ageing in Producing Adenoma-Like Structures in Rats. V. Korenchevsky and S. K. Paris.—p. 903.

Circulation, New York

2:481-616 (Oct.) 1950

*Vulvular Pulmonic Stenosis with Intact Ventricular Septum and Patent Foramen Ovale. Report of Illustrative Cases and Analysis of Clinical Syndrome. M. A. Engle and H. B. Taussig.—p. 481.
Hypertensive Syndrome with Relative Adrenal Cortical Overactivity. D. F. Davies and H. E. Clark.—p. 494.
Nature of Pressor Substances in Pheochromocytomas. D. M. Pitcairn and W. B. Youmans.—p. 505.
Effect of Strophanthus on Coronary Blood Flow and Cardiac Oxygen Consumption of Normal and Failing Human Hearts. R. J. Bing, F. M. Maraist, J. F. Dammann Jr. and others.—p. 513.
*Age, Serum Cholesterol and Coronary Artery Disease. M. M. Gertler, S. M. Garn and E. F. Bland.—p. 517.
Effect of Desiccated Thyroid on Plasma and Tissue Lipids and Atherogenesis in Stilbesterol-Treated Chick. J. Stamler, A. J. Miller, L. Akman and others.—p. 523.
Efficiency of Heparin in Retarding Media on Maintenance of Decreased Coagulability of Blood. H. I. Glueck, C. L. Podore and J. E. Levinson.—p. 530.
Metabolism of Lactate and Pyruvate in Children with Congenital Heart Disease. R. J. Havel and E. Watkins Jr.—p. 536.
Pathology of Pulmonary Vascular Tree: I. Comparison of Intrapulmonary Arteries in Eisenmenger Complex and in Stenosis of Ostium Infundibuli Associated with Biventricular Origin of Aorta. W. H. Civin and J. E. Edwards.—p. 545.
Hemodynamic Study of Case of Anomalous Pulmonary Venous Drainage. W. Hwang, O. Prec, K. Kuramoto, and others.—p. 553.
*Survival to Age of 75 Years with Congenital Pulmonary Stenosis and Patent Foramen Ovale. P. D. White, J. W. Hurst and R. H. Fennell.—p. 558.
Pulmonary Artery Aneurysms. Report of Case Treated by Surgical Intervention. B. Blades, W. Ford and P. Clark.—p. 565.
Electrokymographic Studies of Left Atrium in Normal and Diseased Hearts. J. B. McKinnon and B. Friedman.—p. 572.
Normal Esophageal and Gastric Electrocardiograms. Description, Statistical Analysis and Bearing on Theories of "Electrocardiographic Position." A. D. Kistin, W. D. Brill and G. P. Robb.—p. 578.
RS-T Segment Displacement in Induced Coronary Insufficiency as Studied with Esophageal Leads. L. Scherlis, A. A. Sandberg, J. Wener and others.—p. 598.
A-V Conduction in Auricular Flutter. M. Besoain-Santander, A. Pick and R. Langendorf.—p. 604.

Valvular Pulmonic Stenosis with Intact Septum.—Engle and Taussig present three cases that illustrate the clinical syndrome of valvular pulmonic stenosis with patent foramen ovale. Heretofore, correct diagnosis was rarely made before death. The clinical picture of this malformation is characteristic enough to permit its accurate diagnosis during life. The salient features of the clinical syndrome are delayed onset of cyanosis, dyspnea that is usually greater in severity and

earlier in appearance than is cyanosis, failure to assume knee-chest position after easily induced fatigue, a precordial bulge, an enlarged heart with pulmonic systolic murmur and a weak second sound and an enlarged and pulsating liver. Further features of the syndrome are revealed through fluoroscopy, electrocardiogram, angiocardiogram and catherization of the right side of the heart. The authors emphasize the fact that the malformation must be differentiated from the tetralogy of Fallot, from Ebstein's anomaly of the tricuspid valve, from cor pulmonale and also from the Eisenmenger complex. Correct diagnosis is important, for patients with this malformation may be helped by valvulotomy.

Age and Serum Cholesterol.—Gertler and his co-workers determined serum cholesterol in 146 healthy, working males and 95 males who had had myocardial infarction prior to the age of 40. The control group and the coronary disease group were similar in age, ethnic and racial origin and occupation. A significant positive correlation was found between age and total serum cholesterol level. The rise in the level occurred between the third and sixth decades in both the healthy control group and the coronary disease group. The latter group had definitely higher and more variable serum cholesterol levels than the healthy group at every age group between the third and sixth decades. The authors also determined that (1) in both health and coronary artery disease the cholesterol-phospholipid correlation is high, independent of age; (2) the correlation of age and cholesterol disappears when the influence of phospholipids is removed, and (3) the phospholipids in healthy persons tend to remain correlated with age, but may not do so in the case of coronary artery disease complications. The authors conclude that serum phospholipids are of importance in the normal aging process and, particularly, in coronary artery disease.

Survival with Congenital Pulmonary Stenosis.—White and his associates report the case of a woman with congenital pulmonary stenosis with a patent foramen ovale who survived to the age of 75. Her long survival was probably aided by familial longevity as well as to the fact that she lived a careful life and was not under any severe strain. Moreover, the evolution of her signs suggested that the pulmonary stenosis may have slowly increased in degree in the course of years. The compensation received through the bronchial circulation, as found by the injection of the blood vessels of the lungs, was undoubtedly an important factor in her survival. She lived a useful life, and it is noteworthy that she had no actual heart failure until a few months before death and that her cerebral circulation was maintained satisfactorily until a few weeks before death, when she began to have syncopal attacks. The longest survival period with this disease previously recorded was that of a patient who died at the age of 57 and in whom diagnosis of the disease was made at autopsy.

Delaware State Medical Journal, Wilmington

22:239-282 (Sept.) 1950. **Partial Index**

Cancer Program of the State Board of Health: Report No. 4. W. H. Bandy.—p. 239.
Cardiovascular Disease Program. G. F. Campana.—p. 241.
Is Congenital Syphilis a Problem in Delaware? W. L. Porter.—p. 244.
*Dietary Versus Blood Cholesterol. M. T. Davenport.—p. 247.
Trends in Infant Mortality. C. A. Marshall.—p. 248.
Cleft Palate and Allied Conditions in the State of Delaware from 1940-1950. M. L. Gilmore.—p. 253.
Scope of Physical Therapy in the Crippled Children's Service. M. L. McCarthy and J. L. Wiley.—p. 256.
The Public Health Nurse and the Poliomyelitis Patient. M. M. Klaes.—p. 257.

Dietary Versus Blood Cholesterol.—Davenport cites reports on the feeding of cholesterol to animals and on tests on human subjects that suggest a connection between the synthesis of cholesterol and the endocrine glands. Cholesterol is an ubiquitous, and probably indispensable, constituent of all animal cells. It can be synthesized in the liver from simpler molecules or be supplied by the diet. Elevated blood cholesterol levels tend to be associated with arteriosclerosis, and many different technics can be used experimentally to produce "arteriosclerosis" by raising such levels. It is difficult to cause a lowering of the cholesterol level by dietary restriction. The elevated blood cholesterol levels typical of certain diseases may be caused by disorders of cholesterol synthesis and metabolism rather than by excessive dietary intakes.

Endocrinology, Springfield, Ill.

47:139-218 (Sept.) 1950. **Partial Index**

Effect of Water and Potassium Chloride Ingestion on Level of Urinary 17-Ketosteroids in Rabbit. P. A. Danford and H. G. Danford.—p. 139.
Serologic Behavior of Crystalline Preparations of Hypophyseal Growth Hormone. S. S. Elberg and Choh Hao Li.—p. 143.
Influence of Adrenal Cortex and Thyroid on Loss of Nitrogen in Urine After Experimental Burns. E. A. Sellers, S. S. You and R. W. You.—p. 148.
Effect of Thyroidectomy, Adrenalectomy and Burning of Urinary Nitrogen Excretion of Rat Maintained in Cold Environment. S. S. You, R. W. You and E. A. Sellers.—p. 156.
Effects of Hypophysectomy, Growth and Adrenocorticotropic Hormones on Incorporation of P^{32} into Liver Phospholipids. I. I. Geschwind, Choh Hao Li and H. M. Evans.—p. 162.
Fluorescence Spectra of Natural Estrogens and Their Application to Biologic Extracts. R. W. Bates and H. Cohen.—p. 182.
Lack of Effect of Adrenal Hormones upon Gastric Acid Secretion. H. W. Davenport and V. J. Chavré.—p. 193.

Journal of Allergy, St. Louis

21:373-470 (Sept.) 1950

Effect of X-ray Radiation for Hypersensitiveness. L. H. Criep, L. D. Mayer and S. G. Cohen.—p. 373.
The Aphid—Insect Allergen. G. E. Gaillard.—p. 386.
Skin Sensitivity to Streptomycin. III. S. W. Simon.—p. 400.
Tests of Different Media for Collection and Identification of Air-Borne Saprophytic Fungi. M. A. Swaebly, C. M. Christensen and T. A. Grahek.—p. 404.
Intramural Dissemination of Spores of Hormodendrum Resinae. C. M. Christensen.—p. 409.
Passive Transfer of Cold Urticaria. W. B. Sherman and P. M. Seebohm.—p. 414.
Human Skin Sensitivity to Penicillin G, BT, and O. Demonstration of Cross-Sensitization. G. Risman and W. P. Boger.—p. 425.
Studies on Topical Thephorin Therapy: Index of Sensitization and Effectiveness as Antipruritic. C. Stritzler.—p. 432.

Journal of Lab. and Clinical Medicine, St. Louis

36:501-674 (Oct.) 1950. **Partial Index**

Indican Excretion in Relation to Intestinal Sterilization. W. E. Wooldridge, G. W. Mast and M. Hoffman.—p. 501.
Erythrocyte Survival Studies in Childhood. E. Kaplan and W. W. Zuelzer.—p. 511.
Treatment of Dicumarol-Induced Hypoprothrombinemia in Dogs with Emulsified Vitamin K_1 Administered Intravenously. M. Shoskes, R. P. Geyer, G. S. Yee and F. J. Stare.—p. 531.
Interrelationship of Vitamin B_{12} and Folic Acid in the Baby Pig. B. C. Johnson, A. L. Neumann, R. O. Nesheim and others.—p. 537.
Studies on Experimental Histoplasmosis: IV. Comparison of Virulence of Five Strains of Histoplasma Capsulatum by Intracerebral Inoculation of Male DBA Line 1 Mice. A. Howell and G. F. Kipkie.—p. 547.
Prophylaxis and Treatment of Acute Respiratory Diseases with Antihistaminic Drugs. Personnel of United States Naval Medical Research Unit. No. 4.—p. 555.
Metabolism of Tyrosine in Experimental Megaloblastic Anemia and in Scurvy in Monkey. R. J. Salmon and C. D. May.—p. 591.
Excretion Kinetics of Dye T-1824 in Relation to Plasma Volume Determinations. A. E. Lewis and R. D. Goodman.—p. 599.
Protein Metabolism in Chronic Illness: Effect of Protein Supplementation on Nitrogen Balance, Hemoglobin, Serum Proteins and Weight in the Malnourished and Effect of Nutritional Status on Nitrogen Storage. S. O. Waife, M. G. Wohl and J. G. Reinhold.—p. 604.
Nature of Lesions Encountered in Routine Chest X-Rays. R. V. Slattery, W. G. Beadenkopf and C. G. Loosli.—p. 617.
*Effect of Food and Antacids on Blood Levels of Aureomycin and Terramycin. J. C. Michel, R. J. Sayer and W. M. M. Kirby.—p. 632.
Occurrence of False Positive Tests for Albumin and Glucose in Urine During Course of Massive Penicillin Therapy. R. L. Whipple Jr. and W. L. Bloom.—p. 635.
Tyrosine Metabolism in Infantile Scurvy. C. W. Woodruff.—p. 640.

Effect of Food and Antacids.—Michel and co-workers point out that although aluminum hydroxide gel (amphojel®) has been successfully employed to counteract the nausea and vomiting that may occur with aureomycin therapy, it has been found that the simultaneous administration of aluminum hydroxide gel and aureomycin causes a pronounced depression in serum levels of this antibiotic. Nausea and vomiting remain a problem also with terramycin. The authors studied the effect of three compounds, aluminum hydroxide gel (amphojel®),

basic aluminum carbonate gel (basaljel®) and aluminum phosphate gel (phosphaljel®) and also the effect of food on terramycin and aureomycin serum levels. Simultaneous ingestion of any of the antacids with either antibiotic caused a decided decrease in blood levels. Simultaneous ingestion of food caused no significant alteration in blood levels and appears to be a more appropriate method of controlling nausea and vomiting.

Journal of the Mount Sinai Hospital, New York

17:149-206 (Sept.-Oct.) 1950

Pool of Miscible Uric Acid in Normal and Gouty Man, Studied with Aid of Isotopic Nitrogen. D. Stetten Jr.—p. 149.
Sodium, Water and Edema. J. P. Peters.—p. 159.
Thrombophlebitis Secondary to Acute Respiratory Infection. R. S. Wallerstein.—p. 176.
Gallstone Obstruction of Duodenum: Case Report. R. M. Alexander. —p. 183.
Case of Coexistent Benign and Malignant Bone Tumors. J. F. Katz and F. M. Marek.—p. 187.
Mouth in Diabetes Mellitus. E. Knishkowy, P. Person and H. Pollack. —p. 192.

Journal of Nutrition, Philadelphia

24:1-156 (Sept.) 1950

Nutrition Survey of Tests in Bataan, Philippines. H. B. Burch, J. Salcedo Jr., E. O. Carrasco and others.—p. 9.
Observations on Unknown Dietary Factor Essential for Human Growth. S. E. Snyderman, L. E. Holt Jr., R. L. Nemir and others.—p. 31.
Further Studies on Role of Potassium in Growth and Bone Formation. M. B. Gillis.—p. 45.
Effect of Dietary Level of Tocopherols on Their Metabolism in Swine. J. W. Bratzler, J. K. Loosli, V. N. Krukovsky and L. A. Maynard. —p. 59.
Excretion of Amino Acids in Normal and Undernourished Human Subjects Following Single Infusion of Amino Acid Preparation. S. Level, E. D. Hoganson, J. E. Harroun and C. J. Smyth.—p. 71.
Effect of Fluoride and Grapefruit Juice on Etching of Teeth. A. J. Spencer Jr. and L. N. Ellis.—p. 107.
Contributions of Brewers' Yeast to Diet Deficient in Reproductive Factors. R. E. Nell and P. H. Phillips.—p. 117.

New England Journal of Medicine, Boston

243:513-548 (Oct. 5) 1950

*Chronic Relapsing Febrile Nodular Nonsuppurative Panniculitis (Weber-Christian Disease): Relation to Rheumatic Fever and Allied Diseases. J. C. Brudno.—p. 513.
*Postoperative Potassium Deficit and Metabolic Alkalosis. L. P. Eliel, O. Pearson and R. W. Rawson.—p. 518.
Needs in Field of Psychologic Appraisal of Children with Cerebral Palsy. E. Denhoff.—p. 524.
Mid-Century Trends in Cesarean Section. M. Woodman.—p. 528.
Tuberculosis. D. S. King.—p. 530.

Weber-Christian Disease.—Brudno reports chronic relapsing febrile nodular nonsuppurative panniculitis (Weber-Christian disease) in a woman aged 29. The clinical and microscopic picture was typical of the disease. There was a history of rheumatic fever and of sensitivity to drugs. Although the occurrence of rheumatic fever and nodular nonsuppurative panniculitis in the same patient may have been coincidental, there is the possibility that the two diseases have a common background. The author's theory is that in nodular nonsuppurative panniculitis the antigen-antibody reaction may destroy the cell membrane and liberate free fat. The antigen, which originally may be a chemical, a protein or a bacterial product, stimulates formation of an autoantibody. The autoantibody, reacting with the antigen or antigen-complex in the fatty tissues, leads to nodular panniculitis. This disease is regarded not as a disease entity but rather as an allergic systemic reaction to nonspecific stimuli, with focal manifestations in the subcutaneous or intraperitoneal fat, resulting in destruction of the supporting framework of the fat cell and liberation of free fat. Nodular panniculitis is probably allied to the group of collagen diseases.

Postoperative Potassium Deficit.—Eliel and co-workers report on 32 patients who had undergone major surgical procedures for excision of suspected or proved neoplasms and who presented a postoperative syndrome characterized by apathy, lethargy, nervousness and irritability, muscular weakness, abdominal distention and occasional ileus, occasional confusion, disorientation, delirium, muscular twitching and tetany, electrocardiographic changes and occasional arrhythmia and edema. Hypochloremia, hypoproteinemia and, often hypophosphatemia were observed on blood examination. A prompt reversal of the clinical and blood chemical abnormalities occurred with administration of adequate amounts of potassium. The syndrome developed primarily in patients who were being fed parenterally and who received little or no potassium. Intracellular potassium deficit was demonstrated by balance studies on patients in whom the syndrome developed postoperatively. The deficit arises as a result of renal loss. Losses of potassium from intestinal fluids were small or absent in most cases. Simultaneous radiosodium and bromide spaces showed an excess of sodium over the amount of chloride usually associated with it in extracellular fluid and a tremendous increment in intracellular sodium, which probably replaces cell potassium. The excess of extracellular sodium over chloride determines the observed alkalosis. Diminished erythrocyte potassium and increased erythrocyte sodium concentrations were observed in several patients after development of the syndrome. Loss of intracellular phosphorus was also demonstrated. Known factors in the pathogenesis of postoperative potassium loss are potassium deprivation, loss of gastrointestinal secretions, large infusions of dextrose or isotonic sodium chloride solution, dehydration and malnutrition. These factors do not adequately account for some of the potassium losses observed. Evidence is presented that adrenal hyperfunction resulting from surgical trauma leads to potassium deficit. The clinical and electrolyte disturbances seen in the syndrome resembled those described in some cases of Cushing's syndrome. Metabolic alkalosis and potassium deficit were frequently produced by the injection of pituitary adrenocorticotropic hormone (ACTH) and cortisone (compound E), and there was a striking resemblance between other metabolic changes seen postoperatively and those associated with adrenal hyperfunction. It is suggested that adrenal hyperfunction resulting in potassium deficit may occur after any type of tissue injury. Prevention of the syndrome by provision of potassium early in the postoperative period is stressed. The provision of phosphate ion seems also to be indicated.

Pediatrics, Springfield, Ill.

6:329-508 (Sept.) 1950

Weight in Relation to Fetal and Newborn Mortality: Influence of Sex and Color. L. Baumgartner, V. Pessin, M. E. Wegman and S. L. Parker.—p. 329.
Precocious Puberty. C. W. Lloyd, J. Lobotsky and M. Morley.—p. 343.
Studies on Gelatin-Liquefying Properties of Certain Bacteria with Particular Reference to Laboratory Diagnosis of Cystic Fibrosis of Pancreas. D. E. Johnstone.—p. 351.
Aortic-Pulmonary Communication Due to Localized Congenital Defect of Aortic Septum. S. Gibson, W. J. Potts and W. H. Langewisch. —p. 357.
Effect of Infusions of Citrated Plasma on Plasma Citrate Level of Infants. R. Ames, I. Sylim and S. Rapoport.—p. 361.
Hydranencephaly: Clinical Diagnosis: Presentation of Seven Cases. W. B. Hamby, R. F. Krauss and W. F. Beswick.—p. 371.
*Congenital Tuberculosis. F. E. Amick, M. W. Alden and L. K. Sweet. —p. 384.
*Results of Therapy in 265 Cases of Tuberculous Meningitis. A. Galeotti Fiori.—p. 391.
Self-Demand Feeding in First Week of Life. R. W. Olmsted and E. B. Jackson.—p. 396.
Glycogen Storage Disease of Heart: I. Report of Two Cases in Siblings with Chemical and Pathologic Studies. P. A. di Sant'Agnese, D. H. Andersen, H. H. Mason and W. A. Bauman.—p. 402.
Growth and Development of Negro Infants: I. Analysis of Birth Weights of 11,818 Newly Born Infants. R. B. Scott, M. E. Jenkins and R. P. Crawford.—p. 425.
Incubator Care of Premature Infant: Discussion of Optimal Conditions and Current Methods for Their Provision. J. Dancis and H. M. Cardillo.—p. 432.
Erythroblastosis Fetalis: II. Prognosis in Relation to History, Maternal Titer and Length of Fetal Gestation. F. H. Allen Jr., L. K. Diamond and V. C. Vaughan III.—p. 441.
Kernicterus: Etiologic Study Based on Analysis of 55 Cases. W. W. Zuelzer and R. T. Mudgett.—p. 452.

Congenital Tuberculosis.—Amick and his co-workers present the histories of four prematurely born infants with congenital tuberculosis, observed at the Gallinger Municipal Hospital, Washington, D. C., between 1940 and 1949. Three of these infants were born of mothers with acute miliary tuberculosis and apparently contracted the disease by aspiration in utero of infected amniotic fluid. The fourth infant, born to a mother with acute pelvic tuberculosis and tuberculous peritonitis, seems

to have been infected during passage through the birth canal. Two of the infants died, 17 and 54 days after birth. The other two infants were treated by intramuscular injection of streptomycin. The tuberculous infection appears to have been arrested in them. They are in good health at the ages of 18 and 24 months, respectively. The authors recommend that infants born to mothers with acute miliary or pelvic tuberculosis be given frequently repeated tuberculin tests to insure an early diagnosis and adequate treatment.

Tuberculous Meningitis.—Galeotti Flori outlines the treatment of tuberculous meningitis in use at the pediatric service of the University of Florence. Daily intrathecal administration of streptomycin was continued for 40 to 80 days. The daily dose for infants was 20 or 25 mg., for children 30 to 40 mg. and for adults 50 to 70 mg. The dosage was reduced to half if streptomycin was administered intracisternally and to one third if given subdurally or into the ventricles. Streptomycin was given intramuscularly in daily doses of from 200 to 600 mg. These amounts were given in two or three divided doses. The patients also received an Italian sulfone preparation intravenously throughout the duration of the disease, with brief interruptions every month. Paraaminosalicylic acid was used only in the chronic cases in which streptomycin therapy had been continued for several months. Vitamin A was given intramuscularly in doses of 100,000 international units twice a week and 500,000 international units of vitamin D_2 was administered intramuscularly once a week for from four to six weeks. Other supportive measures consisted of blood transfusions, administration of fluids and amino acids and vitamins B and C. From December 1946 through June 1949, 265 patients with tuberculous meningitis were treated. In the first period, which ended July 1, 1947, intrathecal therapy was discontinued too early, and relapses occurred in some instances, rendering the disease chronic and leading to the appearance of blocks and hydrocephalus. In the second period intrathecal treatment was continued until tests of the spinal fluid were negative. In the third period, the circulation of the spinal fluid was evaluated and the diffusion index was determined; then combined intracisternally and intrathecally administered streptomycin therapy was instituted when necessary. In the fourth period, intraventricularly and subdurally administered streptomycin therapy was initiated in patients with supratentorial blocks. The overall mortality in 1948 was 26 per cent. There are now more than 100 patients who had tuberculous meningitis and now have completely normal spinal fluid, without residual change in the central nervous system. These patients are now leading a normal life.

South Carolina Medical Assn. Journal, Florence

46:305-336 (Oct.) 1950

Esophageal Varices: Treatment of Portal Hypertension by Portacaval Shunt. R. W. Postlethwait and V. Moseley.—p. 305.
*Pudendal Block with Hyaluronidase. H. C. Heins Jr.—p. 309.
Management of Tetanus with Mephenesin. V. Moseley, R. R. Coleman and H. Ellison.—p. 311.
Veratrum Viride in Hypertension. C. B. Meador, K. T. McKee and J. A. Boone.—p. 313.

Pudendal Block with Hyaluronidase.—According to Heins, pudendal block is a near perfect anesthesia for delivery and postpartum repair. It produces considerable perineal gaping within three minutes after injection of the anesthetic. This facilitates a low forceps delivery, makes breech delivery easier and minimizes perineal lacerations. The pain of perineal stretching, which is more severe than other pains associated with labor, is avoided with pudendal block. Hyaluronidase was added to increase the diffusion of the local anesthetic agent. The anesthetic mixture is made by addition of one vial of lyophilized hyaluronidase (150 units) and 0.5 cc. of epinephrine (1: 1,000) to 30 cc. of 1 per cent procaine. The needle is passed to the ischial tuberosity, and 5 cc. of anesthetic mixture is placed posteriorly and medially to the tuberosity to anesthetize the perineal branch of the posterior cutaneous femoris nerve. Then the needle is passed horizontally to the ischial spine, and 5 cc. of solution is deposited here to anesthetize the pudendal nerve as it enters Alcock's canal. Next, 5 cc of mixture is infiltrated in the superior portion of the labia minora to anesthetize the perineal branches of the ilioinguinal nerve. The same procedure is carried out on both sides of the perineum. Complete perineal anesthesia is almost instantaneous. The author presents the results of the first 50 cases in which this simplified technic of pudendal block was used. The operator does not have to inject the nerve itself, but infiltration in the vicinity of the nerve will accomplish an effective block. The use of some basic analgesia during the first stage, in combination with the regional block for delivery, has all the advantages and none of the disadvantages of spinal anesthesia.

Southern Surgeon, Atlanta, Ga.

16:933-1038 (Oct.) 1950

Coverage Problem of Injured Extremity. D. W. Robinson.—p. 933.
Sigmoidovesical Fistula: Diagnosis and Recent Advances in Surgical Treatment. C. S. White and C. S. White Jr.—p. 954.
Use of Bone Bank Bone in Bone Surgery. C. R. Rountree.—p. 966.
Spinal Fusion for Scoliosis Employing Refrigerated Autogenous Bone. L. W. Breck and G. H. Millington.—p. 981.
Some Technical Problems Associated with Complicated Malignant Lesions of Colon. C. J. Hunt.—p. 986.
Surgical Treatment of Portal Hypertension: Review of Reported Clinical Experience and Evaluation Based on Consideration of Physiological and Pathological Factors. H. W. Fischer.—p. 996.
Recent Advances in Treatment of Peripheral Vascular Diseases. T. H. Howard Jr.—p. 1016.

U. S. Armed Forces Med. Jour., Washington, D. C.

1:1095-1248 (Oct.) 1950. **Partial Index**

Detection of Early Carcinoma of Uterus. S. S. Sarkisian.—p. 1095.
Treatment of Tinea Capitis with Local Medication. W. C. Marsh. —p. 1105.
Clinical Use of Antibiotics. III: Treatment of Dental Infections. P. H. Long.—p. 1109.
Care of Premature Infants. J. C. W. Campbell.—p. 1115.
Para-aminosalicylic Acid Resistant "Mycobacterium Tuberculosis." Incidence in Cases Treated at Fitzsimons Army Hospital. W. E. Dye and E. H. Gogley.—p. 1137.
Bone Grafting in Saddle Nose. O. W. Wickstrom.—p. 1141.
*Penicillin, an Allergic Hazard. R. L. Gilman.—p. 1155.
Spontaneous Pneumothorax. Observations on 26 Cases. R. K. Moxon. —p. 1157.
Pediatric Excretory Pyelography. G. R. Hamilton and C. A. DeKovessey. —p. 1163.
Treatment of Intolerance to Quinacrine. J. E. Sokal.—p. 1167.
Early Diagnosis of Trachoma. A. Fuchs.—p. 1171.
Meningococcemia. F. G. Greer and F. H. Mowrey.—p. 1179.
Acute Ruptured Appendicitis and Peritonitis with Urinary Symptoms. E. T. Gordon.—p. 1191.
Air Pollution. W. G. Brandstadt.—p. 1195.
Panorama of Naval Medical Research. C. C. Shaw.—p. 1199.

Penicillin, an Allergic Hazard.—Gilman points out that the gravity of the reactions from penicillin are increasing. The urticaria which formerly amounted to little more than cutaneous discomfort is now being replaced by reactions that simulate the serum sickness of former days and suggest that an anaphylactoid phenomenon has made its appearance. Reactions are characterized by chills, fever, prostration, arthritic symptoms and shock. Recovery is prolonged and exacerbations may follow. The author demands a reappraisal of the use of penicillin and says that we must abandon the thought that this antibiotic is a cure-all. The routine use before all operations is unsound and the practice of administering it for complaints which have no infectious cause must be halted.

Western J. Surg., Obst. & Gynecology, Portland, Ore.

58:523-590 (Oct.) 1950

Hysterosalpingography in Study of Sterility. A. W. Holman.—p. 523.
Comparison of Elder and Younger Primiparas. P. H. Arnot and D. R. Nelson.—p. 535.
Intussusception in Infancy and Early Childhood: Ten Year Review of Cases at the Doernbecher Memorial Hospital for Children. M. S. Rosenblatt and H. D. Colver.—p. 553.
Studies in Vitamin C and Protein Metabolism in Surgical Patients on Routine Hospital Diet. M. J. Brown and P. B. Donovan.—p. 560.
Bilateral Wilms' Tumor: Case Report. J. R. Barr and J. W. Schulte. —p. 567.
Pelvic Girdle Mobility During Menstruation. S. W. Cobb and W. F. Mengert.—p. 570.

FOREIGN

British Journal of Dermatology and Syphilis, London

62:395-442 (Oct.) 1950

Variation in Microsporum Canis and Microsporum Audouini. J. Walker. —p. 395.
Xeroderma Pigmentosum of Mild Type. T. E. Anderson and M. Begg. —p. 402.

Journal Obst. & Gynaec. of Brit. Empire, Manchester

57:525-704 (Aug.) 1950

*Maternal Toxaemia and Foetal Ovarian Activity: Preliminary Observations. A. D. T. Govan and C. L. Mukherjee.—p. 525.
Blood Viscosity in Pregnancy. H. F. H. Hamilton.—p. 530.
Rupture of Uterus in Labour Due to Previous Perforation of Its Wall at Curettage. J. Mair.—p. 539.
Chorionic Gonadotrophin in Toxaemias of Pregnancy. J. A. Loraine and G. D. Matthew.—p. 542.
Pulmonary Embolism Complicating Labour. J. G. Dumoulin.—p. 552.
Total Hystero-Vaginectomy. D. C. Racker.—p. 556.
The Ovarian Theca Cell. S. Shippel.—p. 557.
Method of Locating Placenta in Intact Human Uterus by Means of Radio-Active Sodium. J. C. M. Browne and N. Veall.—p. 566.
Foetus Retained in Abdomen Following Uterine Rupture. A. H. C. Walker.—p. 569.
*Treatment of Eclampsia: Preliminary Report on Present Rotunda Treatment of Eclampsia by Soluble Sodium Thiopentone and Concentrated Salt-Free Dextrose Solution, with Particular Referene to Control of Convulsions. O. Browne.—p. 573.
Scotland's Contribution to Progress of Midwifery in Early Eighteenth and Nineteenth Centuries. R. W. Johnstone.—p. 583.
Meigs' Syndrome: Report of Three Cases. J. G. Lawson.—p. 595.
Pelvic Evisceration for Advanced Persistent or Recurrent Carcinoma of Cervix. A. Weinberg and J. B. Kaiser.—p. 605.
Changes in Cervix Uteri Simulating Adenocarcinoma in Two Successive Pregnancies. R. T. Martin and M. Kenny.—p. 608.
Chorea Gravidarum. O. D. Beresford and A. M. Graham.—p. 616.

Maternal Toxemia and Fetal Ovarian Acitivity.—Govan and Mukherjee made microscope studies of the ovaries of 58 stillborn fetuses. Twenty-five of the mothers had toxemia; the remaining 33 cases involved full-term stillbirths due to causes other than toxemia. There were almost no signs of follicular maturation in the ovaries of the stillborn babies of mothers who did not have toxemia, whereas maturation, luteinization and cystic atresia were common in the toxemic group. The degree of follicular maturation appeared to be directly related to the severity of maternal toxemia. It is suggested that these changes are due to gonadotropic activity and are related to the high concentration of gonadotropins commonly found in the maternal blood in toxemia. The maternal gonadotropins are probably of pituitary rather than of chorionic origin.

Treatment of Eclampsia.—Browne describes efforts made at the Rotunda Hospital in Dublin to improve the unsatisfactory treatment of eclampsia. It was found that when only dextrose with isotonic sodium chloride solution was given and when morphine was given alone or with magnesium sulfate as a sedative and anticonvulsant, edema persisted and fits recurred. It was decided to try some other anticonvulsant therapy and to abandon the view that generalized edema was a protective process indicative of an effort by the body to dilute toxins. A case of severe toxemia confirmed the view that fluids should be given in limited amounts in the form of hypertonic dextrose solution without sodium chloride. At present, unless morphine has already been given, the authors omit it and rely on an initial dose of 0.5 Gm. thiopental sodium in 10 cc. of distilled water administered intravenously to prevent another convulsion while preparing and setting up the thiopental-dextrose drip (3 Gm. of thiopental in 1 liter of 10 per cent dextrose solution without saline). If crystals appear, the mixture is discarded and 3 Gm. of thiopental sodium in 1 liter of 5 per cent dextrose solution is used. Omission of the initial dose of morphine should prevent undue respiratory depression; when morphine has already been given, the initial thiopental dosage by intravenous injection should be halved. If the respirations are 12 or less per minute, or if there is cyanosis or the woman is anemic, oxygen is given until the patient's color remains good without it. A closed oxygen apparatus should be available when thiopental is being given. Limitation of the 24-hour fluid intake to 1 to 1.5 liters is most important, and it is preferable to supplement the thiopental dosage by injection from a syringe rather than by increasing the rate of the drip flow.

An asterisk (*) before a title indicates that the article is abstracted. Single case reports and trials of new drugs are usually omitted.

Medical Journal of Australia, Sydney

2:389-428 (Sept. 9) 1950. **Partial Index**

*Epidemiological Aspects of Rubella. S. G. Anderson.—p. 389.
Diagnosis and Prophlaxis of Rubella. H. McLorinan.—p. 390.
Rubella in Pregnancy: The Obstetrician's Problem. W. M. Lemmon. —p. 392.
Allergy of Nose and Throat. R. S. Steel.—p. 394.
Acute Myocarditis. K. M. Bowden.—p. 397.

Epidemiological Aspects of Rubella.—Anderson discusses evidence that indicated maternal rubella as a cause of fetal malformation. The probability that a woman will bear a deformed child if she has had rubella in the first trimester of pregnancy is somewhat less than 50 per cent. Since it has not been possible to grow rubella virus in the laboratory, rubella antibody cannot be measured and the immune status of a patient cannot be ascertained. This is unfortunate, because a negative history of rubella is often of little value for determination of the immunity of a patient. The failure to grow rubella virus in the laboratory means also that experimental investigation of this disease must be confined to work with human volunteers. In an attempt to solve the problem of active immunization of girls before marriage, studies were made on university women who volunteered for the experiments. The virus in the form of throat washings was taken from rubella patients on the first day of the rash. This material, sprayed into the respiratory tract of susceptible girls, produced rubella. The results indicated that the agent causing rubella is a virus that can be stored at — 70 C., at which temperature it will remain infective for at least two years. The incubation period of the experimental disease ranged from 13 to 20 days. The experimental disease was infective for susceptible contacts. There was evidence that rubella could produce a subclinical infection. Nine subjects with a history of rubella six to nine years previously were not susceptible to the disease. It was concluded that immunity to rubella would probably follow experimental infection. The author feels that these observations justify the offering of rubella infection to all apparently susceptible girls at about 18 years of age. Those who had been purposely infected should be isolated from the community for 10 days.

Annales Paediatrici, Basel

175:285-348 (Oct.) 1950. **Partial Index**

*Treatment of Pneumonia in Children with Single Massive Dose of Sulfathiazole. C. Friderichsen and T. Walther.—p. 285.
Congenital, Familial, Nonhemolytic Icterus: Preliminary Report. E Stransky.—p. 301.
Otogenic Digestive Disturbances: Clinical Observations. P. Rohmer, E. Schneegans and C. Wild.—p. 308.
Congenital Calcificating Chondrodystrophy. W. Swoboda.—p. 322.

Single Massive Dose of Sulfathiazole in Pneumonia.—Friderichsen and Walther report on the use of a single massive dose of sulfathiazole in the treatment of 1,500 children with pneumonia. Of this total, 875 children had pneumonia and 625 had different types of febrile bronchitis. The single massive dose was computed on the basis of 0.3 Gm. of sulfathiazole per kilogram of body weight. Usually, a child was not given more than 4 Gm. (8 tablets) even when the weight exceeded 13 Kg. Only in exceptional cases has the massive dose been as high as 5 Gm. (in strong children 10 or 11 years old.) The tablets were powdered, mixed with saccharine or sugar and dissolved in two tablespoonfuls of water, milk or fruit juice. The patient is allowed to wash the medicine down with a little fluid. The patient is given nothing to eat or drink for four hours after ingestion of the drug. If he is thirsty, 2 to 3 spoonfuls of water are given. After this period the patient is given all the water he desires. As a rule, he falls into a deep sleep soon after the administration of sulfathiazole. In particularly severe cases, in which the fall

in temperature is not satisfactory, a new massive dose is given after 24 or 48 hours. If the child vomits the solution immediately, the same dose is given again after about an hour. The administration of a single massive dose exerted no unfavorable influence on either blood or kidneys. If no satisfactory decrease in fever is obtained during the 24 hours after the administration of the massive dose, the development of complications must be suspected. Suppurating otitis media is a common complication, particularly in young children. Recurrence of pneumonia was observed in 4.1 per cent of cases. The total mortality rate among the 875 cases was 4.9 per cent, but, when those who died within the first 24 hours after admission and those who had congenital defects are eliminated, the death rate was only 0.46 per cent.

Medizinische Klinik, Munich

45:1129-1160 (Sept. 8) 1950. **Partial Index**

*BCG Vaccination: Personal Experiences Based on Nearly 7,000 Vaccinated Children. K. Breu.—p. 1129.
*Observations on Treatment of Congenital Syphilis with Penicillin. W. Reinhard.—p. 1133.
Contribution to Problems of Relationship Between Rhesus-System and Familial Congenital Enterobronchopancreatic "Dysporia" (Glanzmann). H. Bindewald.—p. 1137.

BCG Vaccination.—Breu vaccinated, with the aid of the Danish Red Cross, 6,250 children in the district of Ludwigsburg. These children represented 60 per cent of all tuberculin-negative children between the ages of three and nine years. Control examinations with 33 units (0.33 mg.) of tuberculin for the Mantoux test and, when needed, with up to 100 units of tuberculin (1 mg.), showed that 98.7 per cent of the vaccinated children were tuberculin positive. Control examinations should be made only eight to 12 weeks after the vaccination, since allergy develops only within this interval. General disturbances, such as those associated with antityphoid vaccination, were not observed. A few children had temporary, mild disturbances, such as rise of temperature and anorexia. Roentgen examination of at least 5,000 BCG-vaccinated children demonstrated that no child has so far acquired progressive intrathoracic tuberculosis. Only two children, aged seven years, had a benign primary complex, one of them with involvement of bronchial lymph nodes but without pulmonary involvement. None of the others (at least 80 per cent of the vaccinated children were examined roentgenographically) presented any tuberculous changes in the lungs or hili on roentgenologic examination. The BCG vaccination thus proved to be innocous. The follow-up period is still too short to permit definite conclusions concerning the effectiveness of the vaccination. Experience outside of Germany showed that the incidence of tuberculosis in nonvaccinated tuberculin-negative persons is five to 20 times higher than in the vaccinated persons and that the mortality rate of tuberculosis in the nonvaccinated persons is six to 10 times higher than in the vaccinated. Of 84 children in Ludwigsburg who required treatment for tuberculosis within 10 weeks after vaccination had been done, 81 were not vaccinated and only three had been vaccinated. The author believes that selection of persons to be vaccinated should include tuberculin-negative children and young persons exposed to tuberculosis in their families. Of those not exposed, infants and young adults should be selected, provided they are tuberculin negative. Proof of the absence of tuberculous infection must be obtained in each case with graduated doses of tuberculin. A dose of 100 units (1 mg.) should be used for children who come from a tuberculous environment. These children should be isolated for six weeks before vaccination and for six weeks after infection to prevent a superinfection during the preallergic phase.

Penicillin in Congenital Syphilis.—Reinhard treated 23 children with congenital syphilis with penicillin. Infants aged up to 6 months were given 20,000 units by mouth every two hours for seven and a half days, with a total dose of 1,800,000 units. Infants between the ages of 6 and 12 months were given 30,000 units by intramuscular route every three hours for seven and a half days, with a total dose of 1,800,000 units. Children aged over 1 year received 50,000 units by intramuscular route every three hours for seven and a half days, with a total dose of 3,000,000 units. The only side reaction at the start of treatment was rise of temperature to near 40 C. (104 F.). Syphilitic lesions of the skin and mucous membranes disappeared rapidly. Regression of recent roentgenologic bone changes required two to four months, depending on the severity of the lesion. Serum reaction of the patients became negative within several months after discontinuation of treatment. Negative serum reactions could not be obtained, or with difficulty only, in patients in whom treatment was instituted several years after birth. Recurrences had not been observed when the report was written.

Münchener medizinische Wochenschrift, Munich

92:1081-1160 (Oct. 13) 1950. **Partial Index**

Diagnosis and Treatment of Pheochromocytoma. H. Hindemith and M. Rohde.—p. 1081.
Pathogenesis of Arsphenamine Polyneuritis. K. A. Jochheim.—p. 1093.
New Methods in Treatment of Epilepsy. V. Ziehen.—p. 1097.
Classification and Nomenclature of Dusts and of Organic Changes Caused by Dusts. A. Winkler.—p. 1113.
*Therapeutic Experiences with Vitamin T in Infants. H. Bühl.—p. 1130.

Vitamin T Therapy in Nurslings.—Goetsch, according to Bühl, discovered in 1945 a substance, which when given to insects during their period of growth results in the development of giant types. The substance was extracted from the fat of these insects and from the fungi and yeasts on which these insects fed. The vitamin T used for clinical tests is produced from the yeast Torula utilis. Goetsch demonstrated that this preparation increases growth in higher animal species as well. Nussbaumer used the vitamin T complex in infants with atrophic and dystrophic conditions with favorable results. It is believed that the vitamin will have a stimulating and regulating effect on growing and regenerating tissues. Bühl used the vitamin T complex in 40 infants whose convalescence was retarded and who showed signs of dystrophy or atrophy after disorders in nutrition or after other diseases. The vitamin was given in doses of 2 or 3 drops each day after meals. The preparation has a spicy taste and odor and causes no aversion. Lack of efficacy in the early therapeutic trials is explained by the small doses. The dosage now is 8 drops twice or three times a day, for about four weeks. The weight increase caused by the substance continues for a time after cessation of treatment. Results of treatment were good in 19 cases and were poor in four patients.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

94:2585-2652 (Sept. 9) 1950. **Partial Index**

Perforation of Hilus Lymph Nodes as Cause of Weakly Positive Sputum in Tuberculosis. J. K. Kraan and C. Westerbeek.—p. 2588.
*Prognosis of Tetanus. J. Bonnet.—p. 2595.
*Encephalomyelitis After Cowpox. J. T. Schreuder, T. G. van Rijssel and J. D. Verlinde.—p. 2603.

Prognosis in Tetanus.—Bonnet reviews observations on 44 patients with tetanus. He stresses the prognostic importance of the length of the incubation period. When the incubation period is six days or shorter, the outcome is always fatal; when it is nine days or longer, it is favorable. It is doubtful in those in whom the incubation period is seven or eight days. In these doubtful cases the so-called invasion stage and the temperature may be of decisive significance. The author defines as invasion stage, the time that elapses between the appearance of first symptoms and of the first convulsions. If this period is shorter than four days, the prognosis is unfavorable and death results in a high percentage of cases. If the invasion stage is longer than four days, a fatal outcome is unlikely. There were few fatalities among those in whom the rectal temperature was 38 C. (100.4 F.) or less, but seven of the eight in whom the average rectal temperature was 38.6 C. (101.5 F.) died. The nature and the location of the wound or the patient's general condition on admission are far less decisive for the prognosis than are the invasion stage and the rectal temperature. The author feels that too little attention is given to these factors when the therapy is evaluated.

Encephalomyelitis After Cowpox.—Schreuder and his associates describe clinical and pathological observations on a girl aged 16 who died of encephalomyelitis resulting from cowpox, which she contracted from milking cows with "sore udders." She had helped with the milking for six days because the hands of other milkers had become sore. She began to feel ill on the third day. She had not been vaccinated. She died in coma 18 days after the onset of symptoms. The culture of the spinal fluid revealed no tubercle bacilli. The virus of cowpox was demonstrated in the pustules on the udders of the cows and the vesicles on the hands of the patient. It was not possible, however, to demonstrate the virus in the brain tissue. Results of examination of the virus suggested that the cowpox virus is not identical with the vaccinia virus that is used for human vaccination against smallpox.

Nordisk Medicin, Stockholm

44:1427-1470 (Sept. 8) 1950. **Partial Index**

*Diagnosis and Treatment of Hypoparathyroidism. E. Evang.—p. 1432.
Treatment of Asphyxia of Newborn. J. A. Abolins.—p. 1436.
Fetal Movements and Nervousness. B. Beskow.—p. 1443.
Treatment of Hypertrophy of Prostate in Bispebjerg Hospital. A. Gammelgaard.—p. 1444.

Diagnosis and Treatment of Hypoparathyroidism.—Evang reports on eight women with hypoparathyroidism. All had previously been operated on for goiter. Symptoms of tetany occurred in six patients immediately or soon after the strumectomy. In two patients eight and 10 years elapsed between the operation and the manifestations of hypoparathyroidism. Psychic disorders were present in six patients, who were unstable, irritable and periodically more or less depressed. Treatment with calciferol was given; except in the acute phase, only one patient received a supplement of calcium. The maintenance dose varied from 1.67 to 3.75 mg. of calciferol. Six patients were under complete control, one had paralysis agitans, and one was not willing to follow directions but varied the dose according to her own wishes. Treatment of hypoparathyroidism can be carried out more cheaply with calciferol than with clinically comparable doses of dihydrotachysterol.

Rev. Española Enferm. Aparato Digest., Madrid

9:435-536 (July-Aug.) 1950.

*Prolapse of Gastric Mucosa into Duodenal Bulb. C. Bonorino Udaondo, V. d'Alotto and E. Cabanne.—p. 435.
*Treatment of Peptic Ulcers: Results Obtained with Extracts of Stomach and Small Intestine. F. Flores Olloqui.—p. 444.
Multiple Diverticulosis of Digestive Tract. A. Rocha and A. Guarner.—p. 460.
Syphilis of Stomach. D. Castro-Nuño.—p. 471.
Hydatid Cyst of Gallbladder Simulating Carcinoma. V. Soldevilla.—p. 484.

Prolapse of Gastric Mucosa into Duodenal Bulb.—Bonorino Udaondo and his associates present observations on five instances of prolapse of the gastric mucosa into the duodenum. The clinical symptoms varied greatly. There were complaints of pains and discomfort in the upper abdomen, sometimes combined with a sensation of fulness, particularly after solid and coarse foods were eaten. These symptoms may assume a progressive character and may result in vomiting and disturbed bowel function, or symptoms of obstruction may develop. Physical examination generally does not furnish much diagnostic information. It may reveal deep sensitivity and in rare cases a mobile, bland mass in the region of the pylorus. Roentgenoscopy has been found most helpful in the diagnosis by several investigators, and the authors were able to corroborate this in their cases. The various degrees of prolapse determine the intensity of the roentgenologic and clinical signs. First, transverse folds can be seen in the antrum; these move toward the pylorus. During the so-called antral systole there is a contraction that transforms the transversal into longitudinal folds. After that, with complete filling, the mushroom or cauliflower effect is evident, and after evacuation the areolar outline of the base of the bulb can be seen. The etiology of the prolapse of the gastric mucosa has not been clarified. Treatment consists of a bland diet, small, frequent meals and avoidance of condiments and stimulants. Sedatives and antispasmodics, as well as rest and mental relaxation, may be helpful. Surgical treatment should be reserved for severe cases with violent and refractory symptoms.

Gastric and Intestinal Extracts in Treatment of Peptic Ulcers.—Flores Olloqui found that ambulatory treatment of peptic ulcers is not satisfactory and that to insure healing of an acute ulcer it is necessary to keep the patient in bed for at least 15 days. A modified Sippy diet must be continued for a long time. Aluminum hydroxide is the antacid that has produced the best results in the author's experience. Belladonna and barbiturates are the most valuable antispasmodics and sedatives. The author emphasizes the therapeutic value of deproteinized extracts of the mucosa of the stomach and of the small intestine from recently killed animals. He uses water-soluble extracts for injection and insoluble extracts for oral administration. Patients with gastric ulcer are given extracts of the gastric mucosa, and those with duodenal ulcer are given extracts of the small intestine. The author used these extracts in the treatment of 95 patients. The symptoms disappeared rapidly, and the healing of the ulcer niche was more rapid, particularly in patients with gastric ulcers. Callous and penetrating ulcers and those with cicatricial stenosis of the pylorus do not respond satisfactorily to the extracts.

Schweizerische medizinische Wochenschrift, Basel

80:1021-1044 (Sept. 23) 1950. **Partial Index**

*Severity and Importance of Auditory Disturbances Associated with Prolonged Treatment with Dihydrostreptomycin. F. Van Goidsenhoven and R. Stevens.—p. 1021.
Antibiotics in Treatment of Brucellosis. G. Monasterio, G. Gigli and G. T. Sicca.—p. 1024.
Treatment of Carriers of Typhoid and Paratyphoid Bacilli. V. Gorlitzer von Mundy.—p. 1025.
Chronic Hepatonephritis. J. Calvo Melendro.—p. 1026.
Human Diabetes Mellitus and Experimental Diabetes. J. C. Oya.—p. 1028.

Auditory Disturbances and Dihydrostreptomycin Therapy.—Goidsenhoven and Stevens treated 40 patients with tuberculous meningitis or miliary tuberculosis with dihydrostreptomycin sulfate. Doses of 1.5 to 1.8 Gm. were given daily by intramuscular route for 180 or more days. In addition, doses of 50 to 100 mg. were injected by intraspinal route, with a total of about 80 injections. Some of the patients exhibited a reduced auditory acuity at high frequencies in the second month of treatment. Many patients had a partial loss of auditory acuity at lower frequencies from the fourth to the sixth month of treatment, but this loss developed gradually. Only three patients had severe auditory disturbances that developed rapidly during the third month of treatment. Tinnitus was frequently associated with reduced acuity. It is an alarm signal. Tinnitus continued for six months to one year after discontinuation of this therapy. The case was the same in reduced acuity, which frequently became worse after treatment was discontinued. Nineteen patients were treated with streptomycin by intraspinal route and with dihydrostreptomycin by intramuscular route. Duration of treatment and doses administered were similar to those used with dihydrostreptomycin alone. Audiometric tests showed 50 per cent auditory acuity in five patients, 50 to 90 per cent acuity in seven patients and normal hearing in the remaining seven patients. The auditory changes were less important in these 19 patients than in those treated by dihydrostreptomycin alone, but severer than in patients treated with streptomycin alone. Fifteen patients were treated with medium doses of dihydrostreptomycin by intramuscular route alone. Audiometric tests showed a 51.5 per cent and 35 per cent acuity respectively in two of these 15 patients, while not a single patient of those treated by streptomycin alone by intramuscular route showed any impairment of hearing. Dihydrostreptomycin exerts an extremely toxic effect on the cochlear system. This toxicity becomes particularly manifest during prolonged treatment and even with medium doses of the drug when combined intramuscular and intraspinal treatment is practiced. Dihydro-

streptomycin should not be administered by intraspinal route. Prolonged treatment with dihydrostreptomycin by intramuscular route should also be avoided. Treatment with medium doses of dihydrostreptomycin for short periods of time is justified because it is less likely to cause vestibular disturbances.

Semaine des Hôpitaux de Paris

26:3899-3964 (Oct. 10) 1950. **Partial Index**

Experimental Study of Intestinal Perfusion in Dogs and of Its Consequences, in Particular on the Water Balance of Organism. J. Hamburger, B. Halpern and G. Mathé.—p. 3901.
*Conditions of Dehydration and Hyperhydration Determined in Man by Intestinal Perfusion. J. Hamburger, G. Mathé and J. Crosnier. —p. 3918.
Syndromes of Osmotic Dystonia of Blood Plasma: I. Syndrome of Osmotic Hypertonia of Plasma. J. Hamburger, G. Mathé, J. Crosnier and others.—p. 3929.

Dehydration and Hyperhydration by Intestinal Perfusion.—Experiments with intestinal perfusion performed on dogs by Hamburger and co-workers showed that the intestine may be used as a substitute for the kidney for the excretion of nitrogenous substances and that intestinal perfusion may induce considerable disturbance of the water balance. The authors applied the technic of intestinal perfusion to healthy persons and to patients with edema. A sucrose solution at a freezing point of —0.80 C. was used as perfusion fluid in some of the experiments, while in others the perfusion fluid contained sodium bicarbonate and sodium chloride in addition to sucrose. An intravenous injection of thiocyanate was given and the volume of the extracellular fluid determined 75 minutes before the beginning of the perfusion. Successive blood samples were taken at half-hour intervals from the beginning of the perfusion. Determinations of concentration of the blood, hematocrit, proteinemia and resistance of plasma were made. Results showed that a perfusion fluid consisting of a sucrose solution at a freezing point of —0.80 C. produces dehydration in man, provided the rate of administration is more than 1 liter per hour. A perfusion fluid containing about 2 Gm. of sodium bicarbonate and sodium chloride per liter, in addition to sucrose, produces an extracellular hyperhydration if the rate of administration is less than 2,500 cc. per hour, and it produces extracellular dehydration if the rate is more than 2,500 cc. per hour. The intestine may be used as a substitute for the kidney in man not only for elimination of nitrogenous substances but also for the control of the water and mineral balance. The intestine is able to excrete or absorb water and the main electrolytes according to the composition and rate of administration of the perfusion fluid. Experience suggests that in general any syndrome of extracellular hypertonia corresponds to a condition of dehydration or to a tendency to dehydration of the cell sector, whereas with extracellular hypotony hyperhydration or a tendency to hyperhydration of the cell sector may be expected. The condition of extracellular hydration may be best reflected by the thiocyanate space, and the best indications concerning the cell hydration may be provided by the weight, osmotic pressure of the blood plasma and by the determination of the resistivity of plasma. The fact that the intestinal membrane may replace the kidney in its function of excreting water and chlorides suggests the use of intestinal perfusion as an artificial kidney.

Ugeskrift for Laeger, Copenhagen

112:1277-1310 (Sept. 14) 1950. **Partial Index**

Prolonged Pulmonary Tuberculosis. K. Buhl and O. Lassen.—p. 1277.
Three Cases of Asbestosis. J. Frost.—p. 1284.
*Significance of Estrogens in Development of Cancer of Body of Uterus. A. Terp.—p. 1289.
Estrogen Treatment of Osteogenic Metastases. H. Poulsen.—p. 1296.

Estrogens in Development of Cancer of the Uterus.—Terp concludes that while estrogens in themselves cannot be regarded as cancerigenic in man there is evidence that estrogenic action on the endometrium is a preliminary stage in the development of a malignant endometrial process. There is often a coincidence of endometrial cancer with disorders that are symptomatic of an increased and abnormally prolonged estrogen production, and cancer of the endometrium is rarely seen in women who have undergone surgical castration early. The working hypothesis is that causative factors of cancer of the endometrium are not apparent until an average age of 57 and that they have effect only on an actively proliferating mucous membrane, not on a senile, atrophic mucous membrane. Thus, women with increased endogenic or exogenic estrogenic influence of abnormal duration are liable to cancer of the endometrium. While there is no objection to the application of estrogens before the climacterium, estrogenic therapy during menopause holds a potential danger, because it may maintain an endometrial proliferation in women who would otherwise have an atrophic endometrium and thus not be susceptible to possible cancerigenic factors. Estrogen therapy is an important adjuvant in the treatment of climacteric disturbances, but the author strongly advises cyclic administration —three or four weeks' treatment followed by a week with no therapy. With patients having any of the disorders that frequently coincide with endometrial cancer, further reservation is advocated. In all cases, treatment must be carried out with as small doses and over as short a period as possible. If during treatment bleeding becomes more pronounced or changes character, curettage should be done at once. If the microscopic picture suggests malignancy, estrogen therapy may be deferred for three or four weeks and then a second curettage may be performed before total hysterectomy is undertaken; the picture will then usually be clear. Milder climacteric disturbances often respond well to ordinary sedatives and graver disturbances to treatment with testosterone, which can hardly be thought to predispose to cancer of the endometrium.

Wiener klinische Wochenschrift, Vienna

62:581-596 (Aug. 25) 1950

Structure of Erythrocytes. H. Braunsteiner.—p. 585.
*Treatment of Obliteration of Arteries by Resection and Transplantation of Veins. O. Steinhardt.—p. 587.
Treatment of Epilepsy with Hydantoin Derivatives. W. Solms and G. Wallentin.—p. 588.
Impressions and Experiences of an Otologist During Study Tour in the United States. E. H. Majer.—p. 591.

Treatment of Occlusion of Arteries.—Steinhardt treated 12 men between the ages of 23 and 67 with occlusion of arteries by resection of the arteries and transplantation of veins. Highly satisfactory results were obtained in three patients with posttraumatic thrombosis of the brachial, subclavian and femoral artery respectively. The femoral artery was affected in six other patients, and the femoral and popliteal veins in the remaining three patients. The resected portion of the artery varied from eight to 36 cm. in length. The two remaining portions of the involved arteries were joined by a free vein transplant, the adjacent vein being used in the majority of the cases. Temporary edema due to obstruction occurred temporarily in the leg. The saphenous vein was transplanted in two instances. End to end anastomosis was established by turning the vein. Amputation had to be performed in two patients who had large areas of necrosis before the intervention. One of them was a diabetic with an infected wound, the second, aged 47, with a severe thromboangiitis obliterans had had his other leg amputated previously. Perfect operative results were obtained in four more patients. The pulse could be determined down to the periphery. The patients were free of symptoms. Much improvement resulted from the operation in the remaining three patients, with only one of them still having symptoms of claudication after the walking interval was doubled. Impermeability of the transplant and, therefore, thrombosis, was revealed by arteriography in the latter patient. The follow-up period is still too short to permit a late prognosis, but transformation of the transplants in the sense of an arterialization of the wall may be expected. Transplantation of veins is valuable in improving the circulation in an extremity with advanced disease and in delaying threatened grangrene for a longer time than has hitherto been possible.

BOOK REVIEWS

Industrial Toxicology. By Alice Hamilton, M.D., and Harriet L. Hardy, M.D., Physician to the Division of Occupational Hygiene, Massachusetts Department of Labor and Industries, Boston. Second edition. Cloth. Price, $7.50. Pp. 574. Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, 49 E. 33d St., New York 18, 1949.

Any publication by Alice Hamilton on this subject commands the attention of all persons interested in this field. This edition of the original publication, 1934, is not only rewritten but is considerably enlarged. In addition, Dr. Hamilton has associated with her a junior author who, in her own right through experience and proved competence, is well qualified for the undertaking.

The book has 28 chapters; 11 of these are on metals, four on aromatic solvents and three on occupational cancer. There are other chapters on the following subjects: diagnosis of industrial poisoning; asphyxiants: carbon monoxide, carbon dioxide, the cyanides and hydrogen sulfide; the petroleum fatty, aliphatic series; chlorinated hydrocarbons, bromine derivatives of hydrocarbons and methyl iodide; carbon disulfide; turpentine and tobacco; synthetic rubber, plastics and welding; oil folliculitis; radiant energy and stilbestrol.

There is a bibliography of somewhat more than 1,300 references that enhances the value of the book. The index is rather brief. The introduction presents a general statement about the problems of industrial poisoning in an extremely clear and well organized manner, with particular emphasis on the preventive aspects. In addition, Dr. Hamilton follows her usual good sense in bringing into proper perspective the relation between animal experimentation and the application of such data to the interpretation of disease in man. Further, the industrial environmental aspects are clearly stated, with special attention to implications for the engineer and the physician.

There is a splendid discussion of beryllium and of aluminum. The subjects of silicosis and asbestosis, as well as the pulmonary dust diseases in general, are not specifically covered. One does not find the term pneumonoconiosis in the index; however, this is in keeping with the statement of the authors that this is not a comprehensive review of the subject of industrial diseases. The chapters on lead, mercury and chromium are particularly commendable, although, in connection with the latter metal, more emphasis might have been placed on the hexavalent form in relation to human disease. Some other details are omitted in discussion of other subjects; however, the book represents an important common sense approach, emphasizing etiology and passing from principles to case illustrations, presented in a pleasing style. This book should be of immense value, not only to those directly concerned with industrial toxicology, but also to every undergraduate medical student and general practitioner, in fact to all medical men whose practice brings them in contact with industrial workers.

Freud: Dictionary of Psychoanalysis. Edited by Nandor Fodor and Frank Gaynor. With a Preface by Theodor Reik. Cloth. $3.75. Pp. 208. Philosophical Library, Inc., 15 E. 40th St., New York 16, 1950.

This small volume is written by a psychoanalyst for students of psychoanalysis and for the intelligent layman. The authors adhere strictly to the tenets of psychoanalysis as laid down by Freud. The book is more than a dictionary and, in the nature of the material, had to be such. Mere brief definitions would probably not be satisfactory. The authors frequently resort, therefore, to brief but adequate discussions of the freudian terms. Anyone particularly interested in the intricacies of the freudian terminology can safely refer to this volume for information. The authors have done a thorough and conscientious job, and their dictionary can be safely recommended.

The reviews here published have been prepared by competent authorities and do not represent the opinions of any official bodies unless specifically stated.

Acute Head Injury. By Joseph P. Evans, M.D., Ph.D., Associate Professor of Surgery, University of Cincinnati College of Medicine, Cincinnati, Ohio. Publication Number 60, American Lecture Series, A Monograph in American Lectures in Surgery, edited by Michael E. DeBakey, M.D., Professor of Surgery and Chairman of the Department of Surgery, Baylor University College of Medicine, Houston, Texas, and R. Glen Spurling, M.D., Clinical Professor of Surgery, University of Louisville, Louisville, Kentucky. Neurosurgical Division, editor: Barnes Woodhall, M.D., Professor of Neurosurgery, Duke University, Durham, North Carolina. Cloth. $2.25. Pp. 116, with 24 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; The Ryerson Press, 299 Queen St., W., Toronto 2B, 1950.

This book will take its proper rank in this group of publications, which are already familiar to American medicine. The author, a well known neurosurgeon, has, over an extended period of time, made special laboratory and clinical investigation into the problems of craniocerebral injuries, and this publication may be accepted as up to date and authoritative. It is supplemented by a long bibliography of recent publications, and the illustrations, while not numerous, are clear and to the point. The problem is presented in a simple, logical manner, and covers scalp injuries, skull fractures, meningeal hemorrhage and the various types of surgical lesions following such hemorrhage and cerebral trauma. It is in the latter section that the author discusses with freshness and clarity this perplexing problem, with case histories and information from his own investigations. He has also briefly summarized the current opinions of other investigators. There is nothing in the author's argument that could be disagreed with by most neurosurgeons, and the book might well serve as a guide for surgical residents observing emergency surgery in the receiving rooms of hospitals or for neurosurgeons in training.

Cytologic Diagnosis of Lung Cancer. By Seymour M. Farber, M.D., and others. Cloth. $6. Pp. 59, with 60 plates. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; The Ryerson Press, 299 Queen St., W., Toronto 2B, 1950.

This first monograph dealing exclusively with the cytological diagnosis of pulmonary neoplasms appears in time to meet the growing demand for manuals of exfoliative cytology and gives a good over-all picture of what may be expected from cytological diagnosis of cancer in relation to the diseases of the respiratory system. There are chapters on cytological technic, histology and pathology of the respiratory tract, advantages of study of wet smears, identification of nonmalignant and malignant cells, clinical material and data and clinical pathological results. An essential part of the book is contained in the chapter on cytological criteria of malignancy. Here the criteria of malignancy are outlined in a brief and objective manner.

Since exfoliative cytology is a relatively new field, a uniform terminology has not yet been established. Therefore, it is unfortunate that the authors introduce some new terms, such as "malignant hypercornified cells," without adequately defining them.

In the evaluation of clinical and pathological results, the sensitivity of sputum examination is given as 59 per cent in 197 cases of proved bronchogenic carcinoma, with an average of three specimens per patient. In the 110 cases in which five sputum specimens were examined, the sensitivity was as high as 87 per cent. Undoubtedly, all cytologists agree on the necessity of the examination of several specimens in patients with negative smears whenever there is clinical suspicion of a malignant neoplasm. In order to have an objective evaluation of their observations, the examiners deprived themselves of the knowledge of clinical observations. On the basis of results, achieved in various laboratories, it may be expected that in utilization of clinical data a higher sensitivity may be obtained, even when only three specimens per patient are examined.

The book is illustrated by color photomicrographs. It should be welcome to all cytologists and students of exfoliative cytology as a review of previous work on the subject and as a guide for beginners in the field. The difficulty in publishing a book dealing with a new field is well recognized and, therefore, this contribution to the literature on the cytological method of detection of carcinoma of the lung should be greatly appreciated.

Genetics and the Races of Man: An Introduction to Modern Physical Anthropology. By William C. Boyd, Ph.D., Professor of Immunochemistry, Boston University, School of Medicine, Boston. Cloth. $6, Pp. 453, with 52 illustrations. Little, Brown and Company, 34 Beacon St., Boston 6, 1950.

In this book the author presents the relatively new departure of basing anthropology on genetics instead of on the older system of bone measurements and skull conformation. The main thesis is that racial classification by genetic factors is objective and rests on sounder scientific foundations than that based on anthropometric measurements. Furthermore, it is suggested that a thorough knowledge of genetics may eventually permit the tracing of the inheritance and distribution of genes influencing human behavior and thus be of interest to the sociologist and political scientist. Much of the factual material of the book concerns the genetics of blood groups, a field in which the author has conducted extensive research. Emphasis is placed on the value of blood group determination as a means of racial classification not only because of the ease with which the blood group can be determined and the wealth of available knowledge concerning the exact method of its inheritance but also because of its freedom from the stigmata of prejudice.

While this book was written mainly for specialists, the interests of the layman have not been overlooked by publisher and author, and a short note at the beginning indicates sections that may be omitted by the general reader without the value of the book being diminished. These include the somewhat detailed discussion on genetics in the second chapter and the presentation of statistical methods and their application in the appendixes. The presentation of the subject matter is forceful and the material well documented. The volume is provided with an index, and an extensive bibliography follows each chapter.

Eighth Semiannual Report of the Atomic Energy Commission, July 1950. Paper. Pp. 230, with illustrations. United States Government Printing Office, Washington 25, D. C., 1950.

The semiannual reports of the United States Atomic Energy Commission are official organs describing the progress made in the understanding and use of atomic energy. This report is of particular interest to the medical profession, since it deals with radiation hazards and radiation safety. The report points out that safety rules were adequate before the advent of the atom bomb, when about 3 pounds of radium under human control was available in the entire world, but radioactive materials available now are equivalent to millions of pounds of radium, making the former safety rules inadequate. Permissible limits of exposure to various radiations are tabulated for the guidance of the physician and technician working in the presence of "hot" radioactive materials. The role of the "health physicist" is explained. (It is unfortunate that this name was selected for this important technician.) There is a chapter devoted to instruments for detection of radiation and to the use of the instruments. This is a booklet for every physician to use as reference for reliable information on radiation protection.

Neurosis and Human Growth: The Struggle Toward Self-Realization. By Karen Horney, M.D. Cloth. $3.75. Pp. 391. W. W. Norton & Company, Inc., 101 Fifth Ave., New York 3, 1950.

In this volume Dr. Horney has developed her own theories concerning the neurotic process, which differ somewhat from freudian concepts. She describes neurosis as a special form of development, which is the antithesis of normal human growth. It is stated that in stress, a person becomes alienated from his real self and develops instead a false, idealized self, based on pride but harassed by doubts, self-contempt and self-hate. On this basis the author describes the many factors entering into the slowly developing neurosis and the associated reaction formations, which are attempts at solution through "the expansive solution: the appeal of mastery," "the self-effacing solution: the appeal of love" and "resignation: the appeal of freedom." In contradistinction to these automatically developing neurotic solutions, the author describes the road of solution through psychoanalytic therapy. The variability of the responses of a patient in the course of analysis between self-idealization and self-realization are interestingly described.

A chapter on theoretical considerations defines differences in theory between Dr. Horney's present concept and Freud's basic theory of instincts. While Dr. Horney's contribution is of considerable interest from the professional viewpoint, it appears unlikely that a lay reader already in the throes of neurotic conflict will be anything but further confused by an attempt to understand the material presented without professional assistance.

The Nursery School: A Human Relationships Laboratory. By Katherine H. Read. Cloth. $3.50. Pp. 264, with 13 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W.C.2, 1950.

Children develop healthy personalities easily when their security is enhanced by a feeling of being accepted. Acceptance, according to Miss Read, implies neither approval nor disapproval of the child's behavior in the nursery school group. It implies that the teacher, the parent and other adults associated with the child shall take the child as he is in any given situation and attempt to understand the cause of the behavior of the moment before correction is attempted.

Throughout the book, the nursery school situation is used as a laboratory for the study of the child's relations to other children and to other adults with whom he must associate. The central theme of the book is the importance of adult understanding of the child's emotional reaction to each new situation he encounters and the guiding of the child into growth patterns that make him an acceptable personality in his community. This book is designed primarily for student teachers, particularly at the nursery school level, and contains much technical material on psychology, emotional growth and development and patterns of child behavior. This is well illustrated with many case studies. It would also be a valuable reference book for physicians concerned with children in the preschool and early school ages and for parents who are sufficiently interested in the emotional development of their children to take the time and trouble to read a semitechnical volume.

The Closed Treatment of Common Fractures. By John Charnley, B.Sc., M.B., F.R.C.S., Assistant Honorary Orthopaedic Surgeon, Manchester Royal Infirmary, Manchester, England. Cloth. $7. Pp. 190, with 133 illustrations. The Williams and Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1950.

In this day when men are seeking both fame and fortune through the introduction of all manner of gadgets or through the use of pins, screws, nails and staples of various sizes, shapes and materials in the treatment of fractures, it is comforting to have presented to the profession a common sense, beautifully written and illustrated text such as this. Sir Harry Platt adequately appraised this book when he stated in the foreword, "In this stimulating monograph Mr. Charnley has sought to illuminate some of the obscurities of the mechanics of fracture treatment, and he has succeeded in a most vivid fashion, in creating by means of text and illustration, a series of mental pictures—a frame of reference so to say—whereby the young surgeon can get the 'feel' of a fracture; first the anatomy of the displacement, and then that confident 'clinical sense' of precise correction of the deformity which follows a skilful manipulative act of reduction."

This small book should be in the library of every physician who is engaged in the treatment of injuries to the extremities. No safer or more helpful text could be selected for or recommended to the medical student or young house surgeon.

Recent Advances in Ocular Prosthesis. By J. H. Prince, F.B.O.A., F.S.M.C., F.R.M.S. A Companion Volume to "Ocular Prosthesis." Cloth. $4. Pp. 155, with 89 illustrations. The Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1950.

This small volume is intended as a supplement to "Ocular Prosthesis," which was previously published by the author. In it an attempt is made to bring the subject up to date. It will be of interest primarily to the ophthalmic surgeon and to those responsible for the manufacture and fitting of artificial eyes. Various types of integrated implants are described, together with the surgical technic involved. The author is somewhat overenthusiastic about the end results, as integrated implants are still in a transitional stage and cannot be said to be entirely satisfactory in many cases. Extrusion, retraction of the conjunctiva and objectionable discharge are all too common. This presentation is, however, extremely lucid, and the text is well illustrated with many excellent drawings and photographs. Of added interest are chapters on the making of conjunctival impressions, plastic surgery and the materials and methods used for making the prosthesis. Much of this material is new and offers a significant contribution to the art of improving the appearance of the many persons who have lost an eye through injury or disease.

Recent Advances in Diagnostic Psychological Testing: A Critical Summary. With Contributions by Robert E. Harris, Ph.D., and others. Publication Number 81, American Lecture Series, A Monograph in American Lectures in Psychology, edited by Molly R. Harrower, Ph.D. Cloth. $2.75. Pp. 120. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; The Ryerson Press, 299 Queen St., W., Toronto 2B, 1950.

This monograph presents critical reviews of recent applications of diagnostic psychological methods in the fields of counseling, psychotherapy, psychosomatic medicine, psychiatry and child development. Recent advances in the construction of mental tests and the interpretation of these tests are described and discussed in detail. The probable direction of future development of such tests and their application in research fields is considered. Six lectures are included by authors who are stated to be authorities in their particular fields. The consensus of comment made about present testing methods appears to be that many of the present day technics are both cumbersome and awkward and only by simplification of them will it be possible to obtain satisfactory information that can be of greater use both clinically and experimentally. A chapter relating to the problems of diagnostic technics with children is particularly interesting.

Paul Ehrlich: Schöpfer der Chemotherapie. Von Hans Loewe. Band 8, Grosse Naturforscher, herausgegeben von Dr. H. W. Frickhinger. Halfcloth. 9.50 marks. Pp. 235, with 17 illustrations. Wissenschfüliche Verlagsgesellschaft m.b.H., Tübinger Strasse 53, Stuttgart-1, 1950.

This volume is written by one who is well acquainted with Ehrlich, and the material is presented in a sympathetic and intelligent manner. It is a popular work rather than a technical biography. One gains from it a satisfactory viewpoint concerning Ehrlich, his mode of working and his contributions to chemotherapy—especially with regard to the beginnings of this important field. Much space is devoted to the work that led to the discovery of salvarsan 606, or arsphenamine. This book should prove of great interest to many workers in the field of chemotherapy and should be informative to biologic scientists in general.

Recent Advances in Pharmacology. By J. M. Robson, M.D., D.Sc., F.R.S.E., and C. A. Keele, M.D., F.R.C.P. Cloth. $5.50 Pp. 418, with 46 illustrations. The Blakiston Company (Division of Doubleday & Company, Inc.), 1012 Walnut St., Philadelphia 5, 1950.

The authors of this short textbook have capably surveyed some of the recent advances in the field of pharmacology. The greater portion of the book is devoted to a discussion of a variety of new drugs, attention being focused on both their mode of action and the basis for their clinical use. Drugs discussed include anticholinesterases, such as di-isopropyl fluorophosphate (DFP), hexaethyl tetraphosphate (HETP) and tetraethyl pyrophosphate (TEPP); muscle relaxants, such as curare, mephenesin, decamethonium and flaxadil® (1,2,3-tri[diethylaminoethoxy]benzenetriethyliodide); the ganglionic blocking agents, tetraethylammonium and pentamethonium; radioactive isotopes; nitrogen mustards, pteroylglutamic acid and vitamin B_{12}; and many others. In addition, the authors describe briefly newly introduced technics for the study of the action of drugs in the body and their metabolic fate and discuss methods for evaluation of the actions of drugs in man. Both advanced students and practicing physicians should find this book stimulating and informative.

Electrotherapy and Actinotherapy. By E. B. Clayton, M.B., B.Ch., Consulting Physician to the Physical Treatment Department, King's College Hospital, London. Cloth. $3. Pp. 460, with 132 illustrations. The Williams & Wilkins Company, Mount Royal & Guilford Aves., Baltimore 2, 1949.

This presentation of two subjects in the field of physical therapy is based on two previous books by the same author and is designed for use as a textbook for students. In part 1, electrotherapy is treated systematically, beginning with the fundamentals of electricity and progressing through descriptions of electrical equipment to the application of direct current, alternating current and diathermy. In part 2, under "actinotherapy," the author discusses the physics of radiation and the basis of treatments utilizing infra-red and ultraviolet radiations. Part 3 indicates the uses to which electrotherapy and actinotherapy have been put in treating diseases of joints, muscles, bones, the nervous system, the skin and other parts.

This book contains much material of interest and value and will be helpful to many students. It is written in an easy, almost loose style; the illustrations are casual to the point of crudity. These latter characteristics exemplify a trend in recent textbooks, and in the present instance the tendency is so pronounced as to call for comment. In a section headed "Impedance" (page 94), the student, whether he has ever heard of psychology and logic or not, subconsciously hopes to find a formal definition, complete with genus and differentia; if his time is valuable, he expects to find the subject summarized in this way, and he is baffled if he does not. Similarly, the student expects wiring diagrams to use the schematic symbols that have been made familiar to hundreds of thousands of readers by such publications as the *Radio Amateur's Handbook*, and he is delayed and exasperated by improvised substitutes like those used on page 86 and elsewhere in this book. The widespread belief among present day textbook writers that a subject is made easier by omissions and vagueness is to be deplored. The usefulness of the present volume could also be increased by insertion of metric equivalents for quantities now stated in the apothecary system, by distinction between proprietary and nonproprietary drugs and by adherence (in the parts relating to electricity) to the nomenclature that has been developed by the American Institute of Electrical Engineers. This book can be recommended as collateral reading for students in schools for the training of physical therapy technicians.

Psychology: Principles and Applications. By Marian East Madigan, Ph.D., Specialist, Research Department, Milwaukee Vocational and Adult Schools, Milwaukee. Cloth. $4.25. Pp. 403, with 60 illustrations. The C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1950.

This textbook has been prepared to provide students with a brief introduction to psychology, a foundation for the learning process and an understanding of the biologic and social forces concerning behavior. All periods of the life cycle—childhood, adolescence, adulthood and old age—are considered. The text centers on four units: the nature and methods of psychology, the essentials of learning, the biologic and social bases for behavior and personality adjustment. The author introduces the subject with a therapeutic approach with the stated desire to provide the student not only with psychological tools for use with others, but also with constructive insights by which he may improve his own personal adjustment. The book should be of much value to beginning students of psychology, at the level of the student nurse and student social worker.

QUERIES AND MINOR NOTES

HIGH BLOOD SUGAR WITH NO SUGAR IN URINE

To the Editor:—*Please explain why a patient has a blood sugar level of 135 to 200 mg. and no sugar in the urine. This patient has been in the hospital, takes insulin and has a strict diet.* *Perry Parrigin, M.D., Monticello, Ky.*

Answer.—Although the so-called renal threshold for glucose lies usually in the range of 140-160 mg. per 100 cc. of blood, it varies considerably from person to person. It is often somewhat above this level in older persons, and this is particularly true in patients with arteriosclerosis and nephritis. The situation described is not uncommon. The presence of glucose in the urine depends on three factors: (*a*) the level of glucose in the arterial blood reaching the glomeruli, (*b*) the rate of glomerular filtration and (*c*) the rate of reabsorption of glucose in the tubules. In certain patients such as those mentioned above, in whom the rate of glomerular filtration is less than the average normal, the amount of glucose presented to the tubules for reabsorption may be well within the capacity of the latter despite the fact that the blood sugar may be considerably above normal. Hence no sugar may appear in the urine, despite hyperglycemia of the degree mentioned in the question.

VORACIOUS EATING

To the Editor:—*A girl aged 14 eats enormous amounts of food and remains thin, almost to the point of emaciation. She has an excellent scholastic record and no extraordinary behavior mannerisms. At the age of 12 she menstruated a few times regularly, but since then there have been no menses although she has been subjected to much estrogenic therapy. Results of laboratory tests are essentially negative.*

Horace A. Hall, M.D., Newport Beach, Calif.

Answer.—Excessive or voracious eating is commonly observed in adolescents, whether male or female, and, if accompanied by a sufficient degree of activity, need not lead to excessive weight gain. The food requirements of adolescents frequently are underestimated even by physicians. The case in point is probably one such example. However, the physician must make certain that hyperthyroidism and diabetes mellitus are excluded. The irregularity of menstruation is probably not related to weight and food intake and need not be a matter of concern for another year or two.

ULTRAVIOLET LAMP FOR THE HOME

To the Editor:—*What ultraviolet lamp can be used in the home to prevent respiratory infections? What bad effects, if any, could the constant use of the lamp have on members of the family who spend most of the 24 hours in the home?*

H. D. Diessner, M.D., Minneapolis.

Answer.—The booklet "Apparatus Accepted by the Council on Physical Medicine and Rehabilitation of the American Medical Association," published Feb. 1, 1950, lists six makes of germicidal lamps accepted for use under conditions explained in a lengthy statement (pages 118-129). This statement affords no logical basis for the installation of germicidal lamps in the normal home, and there seems to be no published evidence that such lamps will prevent respiratory infections in the family. Lamps sufficiently strong to make a "light curtain" in a corridor can cause burns on calves and ankles (page 121); other untoward effects on eyes and skin are to be expected from prolonged exposure (*J. A. M. A.* **140**:1334 [Aug. 27] 1949; **142**:147 [Jan. 21] 1950).

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any official bodies unless specifically stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

BUBBLE SOAPS

To the Editor:—*Oral ulcers developed in a small boy shortly after he had used a bubble soap to blow bubbles. The label states the material is nonpoisonous. The ulcers subsided within a few days, but I wonder whether there is something in the product that could have caused the ulcers.*

August J. A. Watzlavick, M.D., Schulenburg, Texas.

Answer.—Minor oral ulceration in children is not a rarity and may occur in the absence of any known external irritant. Without particular reference to the product mentioned, it may be noted that many liquid bubble soaps are coconut oil-potassium hydroxide soaps to which are added methyl cellulose and glycerin. The reason for the coconut oil-potassium soap is that this is practically the only true soap that stands up as a liquid. The methyl cellulose and glycerin provide the wanted tenacity for large bubbles, but other substances could be substituted. Of all high grade soaps those containing coconut oil and potassium cause concern owing to their well established skin irritant properties. Methyl cellulose, if present, probably may be ignored as an irritant. All soaps, even though substantially alkali free before use, undergo hydrolysis in the presence of water and invariably yield some alkali but not necessarily harmful amounts. In the instance described, the alkali from hydrolysis may have facilitated the ulceration. To an equal extent this might follow the entry of many other soaps into the mouth.

Materials other than soaps have been promoted for "bubble blowing." Variously these are plastics or synthetic detergents. Some of the plastics require solution in hydrocarbons. At least one proved to be destructive of coated surfaces, such as varnish on furniture and harmful to fabrics such as rugs. On occasion eye injuries have arisen, particularly corneal damage. As between "bubble soaps" and plastic bubble agents, the latter warrant greater concern as to personal injury.

LEUKEMIA IN CHICKENS

To the Editor:—*Please send me any information you can obtain on leukemia in chickens and its relation to humans.*

L. Paul Foster, M.D., Orlando, Fla.

Answer.—The avian leukoses are diseases characterized by autonomous proliferation of the precursors of leukocytes (Brester, H. E., and Schwarte, L. H.: Diseases of Poultry, ed. 2, Ames, Iowa, Iowa State College Press, 1948, p. 421). The term leukosis has largely replaced the older name leukemia, since changes in the peripheral white blood cell count are not always found. Several disease entities are included among the avian leukoses. Their adequate classification is a complex problem, particularly since their etiology has not been fully elucidated. Work done to date indicates that oncogenic viruses are the causative agents of these diseases in fowl. These viruses have never been implicated in the pathogenesis of human leukemia or other diseases of man. These blood dyscrasias of fowl are not transmissible to man.

FALLING OUT OF EYEBROWS

To the Editor:—*What can cause eyebrows and eyelashes to drop out in a 12 year old girl? No particular blepharitis or actual pulling out of the hairs and no baldness elsewhere have been observed? There is regrowth later, according to the history.* *M.D., Kansas.*

Answer.—It may be that this child has alopecia areata, which sometimes attacks eyebrows or eyelashes only; in this disease the hairs may fall out and regrow spontaneously. The cause of alopecia areata is not known, although in many cases there seems to be a link with the emotions. It has also been observed that persons with alopecia areata sometimes require correction of visual defects, and other cases are thought to be due to infected teeth.

SUGGESTIONS FOR MAKING A DIAGNOSIS

To the Editor:—*A girl aged 9 has an illness of gradual onset for five months. Her chief complaints are weakness, dull aching pain across the upper part of her abdomen that has no relation to food intake, occasional nausea without vomiting and a rather persistent fever, with temperature ranging from 99 to 101 F. Her family history is noncontributory. The patient is rather tall for her age, pale and thin. Physical examination disclosed no abnormalities except that both spleen and liver push about 2 inches (5 cm.) below the respective rib margins during deep inspiration. The surfaces of both organs are smooth, and each is slightly tender. Lymph nodes are not palpable. The blood pressure is normal. Results of urinalysis and Wassermann tests are negative. A chest roentgenogram and results of patch test and agglutination tests for brucellosis, typhoid and paratyphoid were negative, as was one blood culture. Red blood cells numbered 3,900,000 and white blood cells 9,000 with 47 per cent lymphocytes. The sedimentation rate (Westergren) was 5 mm. for the first hour. Is it possible to formulate a diagnosis; if not, what tests would you suggest?*

Frank W. Pisciotta, M.D., Highland Park, N. J.

Answer.—As splenohepatomegaly is the only conspicuous physical observation, further search should be made for conditions exhibiting this manifestation. Familial splenic anemia (Gaucher's disease) should be excluded by a sternal puncture and a search made for the typical Gaucher cell, as abdominal pain often accompanies this condition; it usually develops insidiously during the first decade and is most frequently found in girls. Rheumatoid arthritis with splenohepatomegaly occurs after the sixth year of life, with general symptoms and fever, which may be present for weeks or months before definite articular manifestations make their appearance. The type in which enlargement of the spleen and lymph nodes are prominent is known as multiple rheumatoid arthritis (Still's disease). Definite diagnosis without articular manifestations is impossible. Other conditions that might be responsible for the signs and symptoms enumerated are infections such as pyuria (congenital), chronic brucellosis, chronic sinus infection, fungus infection such as histoplasmosis, subacute bacterial endocarditis, malaria and parasitic diseases and chronic sepsis of unknown origin. Further tests that these conditions would suggest are intravenous pyelogram and culture of a catheterized specimen of urine, to rule out pyuria; repeated blood, urine and stool cultures and agglutination tests to rule out chronic infections, or brucellosis roentgenograms to rule out sinus infection; repeated blood cultures to rule out bacterial endocarditis and chronic sepsis; stool examination to detect ova of various parasitic diseases; a blood smear to exclude malaria, and skin tests with histoplasmin to rule out fungus infection. These additional tests are suggested because it does not seem possible for one to formulate a diagnosis on the basis of the information presented.

NO TREATMENT TO IMPROVE QUALITY OF SEMEN

To the Editor:—*I have a patient aged 27 with a sperm count of 30,000,000. Results of his physical examination are essentially normal, and there is no history of venereal infection. Can the sperm count be increased so that the patient might impregnate his wife? She has been thoroughly checked and found to be essentially normal.*

E. W. Ellis, M.D., Elgin, Minn.

Answer.—A sperm count of 30,000,000 is not inconsistent with clinical fertility, provided the morphology and motility of the spermatozoa are good. These items should be checked. There is no treatment that can be relied on to improve the quality of semen in numbers or in any other respect. The most hopeful measures are systematic regulation of hygiene and administration of thyroid in dosage sufficient to keep the basal metabolic rate at or slightly above +10 per cent. If a postcoital examination, or Sims-Huhner test, performed at the wife's ovulation time shows several active spermatozoa per high power field in the cervical mucus, a moderately subnormal sperm count is probably not important on its own merits. If postcoital findings are deficient, material with a high concentration of spermatozoa may be obtained for artificial insemination either by centrifuging an entire specimen of the husband's semen or by taking the first part of a divided ejaculate.

CURRENT USED IN ELECTROCOAGULATION

To the Editor:—*What is the voltage and amperage of the current used in electrocoagulation, electrocutting and electrodesiccation? I wish to know the values after they have been "stepped up" and as they are used at the active electrode, not the original current.* *M.D., New Jersey.*

Answer.—The answer to this question cannot be simple, because the terms "voltage" and "amperage" arise primarily in connection with direct current, whereas the processes of electrocoagulation and the like involve the use of alternating currents. Moreover, the potentials and intensities used must be varied within wide limits because of the varying properties of skin and other tissues. In electrodesiccation and "cold cautery" with a needle, for instance, the voltage of the high frequency current oscillates between +100 and —100 volts about 300,000 (up to 1,000,000) times per second, and the current reverses itself an equal number of times. Since the to-and-fro motions of the current are equal, one cannot speak of amperage in the usual sense, but one can say that the heat produced is equal to that which would be produced by a direct current of, say, 200 milliamperes applied under the same conditions for the same length of time. If the area to be treated is increased, the "amperage" must be increased accordingly to, say, 2,000 or 3,000 milliamperes, and, if the electrode is to be held loosely or out of actual contact with the skin so as to establish an arc, as in electrosection, the "voltage" must be increased so that the potential alternates between +500 and —500 or even between +1,000 and —1,000 volts.

CHRONIC MALARIA

To the Editor:—*In what length of time may one expect to find positive malaria smears in veterans returning from malarial districts? What statistics are available, and in patients with positive reactions what would be the most likely seat of infection?* *E. K. Disney, M.D., Outwood, Ky.*

Answer.—There are a few valid statistics relating to the detection of circulating parasites following the termination of the acute attack, although the patient may still be suffering from chronic malaria. Patients whose disease is in the chronic state are usually sufficiently ill to require some antimalarial drug, and it is difficult to find patients whose blood stream parasites have not been influenced by this medication. One case is known in which circulating parasites continue to be found seven years after the date of the first attack. It is not uncommon for such occurrences to last one to two years. The seat of infection is not known exactly, since positive blood smears mean widespread distribution of the parasites throughout the entire body, but it is commonly assumed that the residual infection resides in the spleen and bone marrow.

RECOVERY FROM TETANUS

To the Editor:—*What is the longest period of time that a patient has been known to have convulsions from tetanus and still live?* *E. T. Drake, M.D., Williamson, W. Va.*

Answer.—Because all cases of tetanus are not reported, a definite answer to this question is scarcely possible. However, a tetanus patient has been known to have convulsions as late as five weeks after the onset of the disease and yet recover eventually.

RETINAL DETACHMENT DURING PREGNANCY

To the Editor:—*In a primipara aged 36, five months pregnant, there developed suddenly an eye condition which is considered to be bilateral detachment of the retina. She has been under the care of competent ophthalmologists, who have treated the condition conservatively. She is due to deliver soon. There is a difference of opinion among the ophthalmologists as to the safest mode of delivery for this patient. Would you consider the physiological variation in blood pressure during and between labor contractions as hazardous to this patient's eye condition? Would cesarean section be the safest method of delivery?*

M.D., California.

Answer:—Most ophthalmologists favor interruption of pregnancy when retinal detachment is present. Meyer Weiner (Diseases of the Eye in Adair, F. L., and Stieglitz, E. J.: Obstetric Medicine, Philadelphia, Lea & Febiger, 1934, p. 330) says that, whereas detachment of the retina as a complication of retinitis unassociated with pregnancy practically always results in blindness, more than half the patients in whom retinal detachment occurs during pregnancy recover with some useful vision. Notwithstanding this, the risk is so great that there is little difference of opinion as to proper action: Pregnancy must be terminated. Since the pregnancy continued in this patient undisturbed and there is no mention of further retinal detachment, there is no harm in permitting the patient to have a vaginal delivery. The labor pains should not have any adverse affect on the patient's eye condition. Of course, as much of the pains of labor as possible should be relieved by analgesic drugs, and the delivery itself should be carried out under direct infiltration anesthesia rather than inhalation anesthesia.

EXPRESSING THE PLACENTA

To the Editor:—*Somehow I gathered the impression that Credé's method of helping in the expulsion of the placenta after the delivery of the child is now an outmoded, if not dangerous, procedure. Is my impression correct? If so, what maneuver is advocated by most obstetricians at present?*

Valdemar O. Zialcita, M.D., San Francisco.

Answer.—The Credé method of expressing the placenta is good practice and in common use. It is now believed that the placenta is separated from the uterus by the rapid contraction of the uterus following the birth of the baby. A new technic has been added, namely, the administration of ocytoxics with the presentation of the shoulder to help the uterus to contract more rapidly, thus minimizing blood loss. Credé's method is safe, but the pressure used should not damage the uterus.

HEMOSTATIC ECZEMA

To the Editor:—*Please tell me the etiology, symptoms, prognosis and treatment of hemostatic eczema.*

J. W. Hopkins, M.D., Glendale, Calif.

Answer.—Hemostatic eczema or dermatitis is that type of eczema which occurs on the legs, supposedly as a result of an impaired vascular supply to the areas. It is sometimes referred to as varicose eczema, statis dermatitis or circulatory eczema, depending on the underlying vascular deficiency. Clinically, like other types of eczema, it may be acute or chronic, papular or vesicular, dry or moist, relatively smooth, thickened or lichenified, and it may occur in patches or with diffuse involvement. It is sometimes complicated by the development of edema, purpura, ulcers or secondary infection with resultant lymphangitis, cellulitis or erysipelas, recurrent attacks of which may produce elephantiasis.

Generalized dermatitis, in the form of an "id" type reaction, may develop. Some physicians believe that nutritional deficiency and foci of infection, particularly infected teeth, play a role in hemostatic eczema. When the eczema is acute, treatment is with bedrest, elevation of the legs and the application of soothing wet packs or lotions. When the acuteness subsides, soothing ointments are substituted. Secondary infection is treated with an antibiotic agent. Contributing factors, such as anemia or nutritional deficiency, should be treated. When the patient is ambulatory, the legs should be encased in supportive elastic bandages, and varicose veins, if there are no contraindications, should be treated by surgical methods and/or injections of sclerosing agents.

IMPROVEMENT WITH THYROID WHILE BASAL METABOLIC RATE REMAINS LOW

To the Editor:—*An 18 year old girl complains of excessive tiredness and has a basal metabolic rate of —25 per cent. The patient's skin is dry and her pulse rate is 66; other results of physical examination are normal. There is no disturbance of menstruation. Six months' medication with thyroid extract, 1 grain (60 mg.) daily, did not improve the basal metabolic rate. The last test, in September 1950, showed a rate of —26 per cent. Subjectively the patient is improved. Can you explain the poor response to the thyroid medication? All tests have been technically correct. Does thyroid in a case like this have to be continued for a definite time?*

M.D., New York.

Answer.—In this patient improvement is claimed from the administration of desiccated thyroid in a dose of 1.0 grain daily, although before treatment was given the basal metabolic rate was —25 per cent and after the administration of thyroid it was —26 per cent. Various possibilities must be considered: 1. Improvement sometimes does occur in patients with small doses of thyroid, even though no change in basal metabolism is noted. 2. Hypothyroidism is not the only cause of a low basal metabolic rate, and in some patients metabolism may be somewhat depressed even though clinical evidence indicates that the thyroid function is normal. 3. The improvement may be psychogenic. In most instances in which the administration of desiccated thyroid produces clinical improvement the basal metabolism changes, but as is already indicated some improvement may occasionally occur without any definite change in the metabolic rate.

PRECOCIOUS PUBERTY

To the Editor:—*I should like to add a more probable diagnosis to the answer given a question concerning precocious puberty in an 8 year old girl in "Queries and Minor Notes" (J. A. M. A. **143**:1381 [Aug. 12] 1950). Polyostotic fibrous dysplasia should be given careful consideration, especially since the girl had fractures of both an arm and a leg. Albright and co-workers described a syndrome characterized by osteitis fibrosa disseminata, areas of pigmentation and endocrine dysfunction (New England J. Med. **216**:727 [April] 1937) and by gonadal dysfunction (Endocrinology **22**:411 [April] 1938). This particular child should be carefully studied roentgenographically to determine whether there is evidence of fibrous dysplasia of the bones and carefully examined for cutaneous pigmentation. The now accepted terminology "polyostotic fibrous dysplasia" proposed by Lichtenstein (Arch. Surg. **36**:874 [May] 1938) is the more general term. It is often associated with the extraskeletal manifestation of precocious puberty in the female. As the jaws are commonly involved, it would be of value to have intraoral roentgenograms taken, and, if these are suspicious of fibrous dysplasia, a biopsy is a simple procedure. Polyostotic fibrous dysplasia is not as rare as once suspected (Neller, J. L.: Osteitis Fibrosa Cystica, Am. J. Dis. Child. **61**:590 [March] 1941. Furst, N. J., and Shapiro, R.: Polyostotic Fibrous Dysplasia: Review of the Literature with Two Additional Cases, Radiology **40**:501 [May] 1943. Albright, F.: Polyostotic Fibrous Dysplasia: A Defense of the Entity, J. Clin. Endocrinol. **7**:307 [May] 1947). Lichtenstein states that it is "the second most frequent systematized anomaly of skeletal development, being outranked only by multiple exostosis." The early diagnosis of this disease entity is of more than academic interest. Pathologists write that there is a paucity of material for study and believe that no progress will be made until sequence material can be studied from an early age.*

Marsh Robinson, D.D.S., M.D., Santa Monica, Calif.